```
Connecting via Winsock to STN


Welcome to STN International'  Enter x:x

LOGINID:ssspta1644axd

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08   "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09   BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09   ZDB will be removed from STN
 NEWS  5  Apr 19   US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22   Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22   BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22   Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03   New e-mail delivery for search results now available
 NEWS 10  Jun 10   MEDLINE Reload
 NEWS 11  Jun 10   PCTFULL has been reloaded
 NEWS 12  Jul 02   FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22   USAN to be reloaded July 28, 2002;
                   saved answer sets no longer valid
 NEWS 14  Jul 29   Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30   NETFIRST to be removed from STN
 NEWS 16  Aug 08   CANCERLIT reload
 NEWS 17  Aug 08   PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08   NTIS has been reloaded and enhanced
 NEWS 19  Aug 09   JAPIO to be reloaded August 25, 2002
 NEWS 20  Aug 19   Aquatic Toxicity Information Retrieval (AQUIRE)
                   now available on STN
 NEWS 21  Aug 19   IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 22  Aug 19   The MEDLINE file segment of TOXCENTER has been reloaded

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *



FILE 'HOME' ENTERED AT 16:19:43 ON 23 AUG 2002

=>  file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:19:59 ON 23 AUG 2002

FILE 'CAPLUS' ENTERED AT 16:19:59 ON 23 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 16:19:59 ON 23 AUG 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'BIOSIS' ENTERED AT 16:19:59 ON 23 AUG 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC. R

=> s Larche m?/au or kay A?/au
L1        2885 LARCHE M?/AU OR KAY A?/AU

=> s l1 and allergen
L2         503 L1 AND ALLERGEN

=>
```

```
=> dup erem l4
ENTER REMOVE, IDENTIFY, ONLY, OR ? :end

=> dup rem l4
```

```
L4   ANSWER 1 OF 1       MEDLINE                  [illegible]
ACCESSION NUMBER:    2001262386      MEDLINE
DOCUMENT NUMBER:     21203301   PubMed ID: 11376488
TITLE:               Mechanisms of T cell peptide epitope dependent
                     late asthmatic reactions.
```

AUTHOR: **Larche M**; Haselden B M; Oldfield W L; Shirley K; North J; Meng Q; Robinson D S; Ying S; **Kay A B**
CORPORATE SOURCE: Allergy and Clinical Immunology, Imperial College School of Medicine, London, UK.. m.larche@ic.ac.uk
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 272-5.
Journal code: 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Short **peptide** sequences corresponding to T cell epitopes have been identified in the major cat **allergen** Fel d 1. In order to directly activate **allergen** specific T cells in cat allergic asthmatic individuals, **peptides** were administered by intradermal injection. Subsequently, a proportion of subjects experienced a delayed reduction of airway calibre manifested as a decrease in FEV(1). Changes in lung function occurred approximately 3 h after **peptide** injection, peaked at 6 h and resembled an isolated late asthmatic reaction (LAR). Using molecular tissue typing techniques, it was determined that many of the individuals experiencing isolated LAR expressed particular **HLA**-DR molecules. These molecules were shown in subsequent experiments to bind individual **peptides** within the preparation and thus to activate T cells in a major histocompatibility complex (**MHC**)-restricted fashion. The precise mechanisms whereby **MHC** restricted activation of **allergen** specific T cells gives rise to bronchoconstriction are currently under investigation. Copyright 2001 S. Karger AG, Basel

TI Mechanisms of T cell **peptide** epitope dependent late asthmatic reactions.

AU **Larche M**; Haselden B M; Oldfield W L; Shirley K; North J; Meng Q; Robinson D S; Ying S; **Kay A B**

AB Short **peptide** sequences corresponding to T cell epitopes have been identified in the major cat **allergen** Fel d 1. In order to directly activate **allergen**-specific T cells in cat-allergic asthmatic individuals, **peptides** were administered by intradermal injection. Subsequently, a proportion of subjects experienced a delayed reduction of airway calibre manifested as a decrease in FEV(1). Changes in lung function occurred approximately 3 h after **peptide** injection, peaked at 6 h and resembled an isolated late asthmatic reaction (LAR). Using molecular tissue typing techniques, it was determined that many of the individuals experiencing isolated LAR expressed particular **HLA**-DR molecules. These molecules were shown in subsequent experiments to bind individual **peptides** within the preparation and thus to activate T cells in a major histocompatibility complex (**MHC**)-restricted fashion. The precise mechanisms whereby **MHC** restricted activation of **allergen** specific T cells gives rise to bronchoconstriction are currently under investigation. Copyright 2001 S. Karger AG, Basel

CT Check Tags: Animal; Human
*Asthma: IM, immunology
Cats
Cell Line
*Epitopes: IM, immunology
Forced Expiratory Volume
Glycoproteins: IM, immunology
HLA-DR Antigens: IM, immunology
Hypersensitivity: IM, immunology
Lymphocyte Transformation
Peptides: IM, immunology
*T-Lymphocytes: IM, immunology

CN 0 (Epitopes); 0 (Glycoproteins); 0 (**HLA**-DR Antigens); 0 (**Peptides**); 0 (**allergen** Fel d I)

L5 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:187752 BIOSIS
DOCUMENT NUMBER: PREV200100187752
TITLE: Attenuation of cutaneous and bronchial late allergic reactions by short **allergen** derived **peptides** is associated with a reduction in **peptide** and whole **allergen** induced T cell effector function.
AUTHOR(S): Shirley, Karen E. [1]; Oldfield, William L. G. [1]; **Kay, A. Barry** [1]; **Larche, Mark** [1]
CORPORATE SOURCE: [1] NHLI Division, Imperial College School of Medicine, London UK
SOURCE: Journal of Allergy and Clinical Immunology, February, 2001) Vol. 107, No. 2, pp. S67. print.
Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001
ISSN: 0091-6749.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Attenuation of cutaneous and bronchial late allergic reactions by short allergen derived peptides is associated with a reduction in peptide and whole allergen induced T cell effector function.
AU Shirley, Karen E. [1]; Oldfield, William L. G. [1]; **Kay, A. Barry** [1]; **Larche, Mark** [1]
CS [1] NHLI Division, Imperial College School of Medicine, London UK
SO Journal of Allergy and Clinical Immunology, February, 2001) Vol. 107, No. 2, pp. S67. print.
Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001
ISSN: 0091-6749.
DT Conference
LA English
SL English
AB Short **peptide** sequences corresponding to T cell epitopes have been identified in the major cat **allergen** Fel d 1. In order to directly activate **allergen** specific T cells in cat allergic asthmatic individuals, **peptides** were administered by intradermal injection. Subsequently, a proportion of subjects experienced a delayed reduction of airway calibre manifested as a decrease in FEV(1). Changes in lung function occurred approximately 3 h after **peptide** injection, peaked at 6 h and resembled an isolated late asthmatic reaction (LAR). Using molecular tissue typing techniques, it was determined that many of the individuals experiencing isolated LAR expressed particular **HLA**-DR molecules. These molecules were shown in subsequent experiments to bind individual **peptides** within the preparation and thus to activate T cells in a major histocompatibility complex (**MHC**)-restricted fashion. The precise mechanisms whereby **MHC** restricted activation of **allergen** specific T cells gives rise to bronchoconstriction are currently under investigation.
CT Human
Asthma: IM, immunology
Cats
Cell Line
Epitopes: IM, immunology
Forced Expiratory Volume
Glycoproteins: IM, immunology
HLA-DR Antigens: IM, immunology
Hypersensitivity: IM, immunology
Lymphocyte Transformation
Peptides: IM, immunology
T-Lymphocytes: IM, immunology
CN 0 (Epitopes); 0 (Glycoproteins); 0 (**HLA**-DR Antigens); 0 (**Peptides**); 0 (**allergen** Fel d I)
IT Anatomy, Cytology, & Organogenesis
Immune System: Respiratory System: Respiratory Homeostasis
IT Parts, Structures, & Systems of Organisms
T cell: **allergen** induced effector function, Blood and lymphatics, immune system, proliferation
IT Diseases
asthma: immune system disease, respiratory system disease
allergen: peptide
MHC (major histocompatibility complex)
IT Alternate Indexing
Asthma (MeSH)

L5 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001-187652 BIOSIS
DOCUMENT NUMBER: PREV200100187652
TITLE: **MHC**-restricted, IgE independent, **allergen peptide**-induced late asthmatic reactions.
AUTHOR(S): **Larche, Mark (1)**
CORPORATE SOURCE: (1) Allergy and Clinical Immunology, Imperial College School of Medicine, National Heart and Lung Institute, London UK
SOURCE: Adorini, Luciano, Arai, Ken ichi; Berek, Claudia; Capra, J. Donald; Schmitt Verhulst, Anne-Marie; Waksman, Byron H.. Chemical Immunology, (2000) Vol. 78, pp. 30-38. Chemical Immunology. Immunological mechanisms in asthma and allergic diseases. print.
Publisher: S. Karger Publishers Inc. 79 Fifth Avenue, New York, NY, 10003, USA.
Meeting Info.: Symposium London, England, UK June 24 25, 1999
ISSN: 1015-0145. ISBN: 3-8055 7112 7 (cloth).
DOCUMENT TYPE: Book Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
TI **MHC** restricted, IgE independent, **allergen peptide**-induced late asthmatic reactions.
AU **Larche, Mark (1)**
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis)
IT Diseases
late asthmatic reaction: **allergen peptide**-induced, immune system disease, immunoglobulin E independent, major histocompatibility complex-restricted, respiratory system disease
IT Chemicals & Biochemicals
allergen peptide; immunoglobulin E; major histocompatibility complex

L5 ANSWER 4 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000 134874 BIOSIS
DOCUMENT NUMBER: PREV200000134874
TITLE: Mechanisms of the late asthmatic reaction induced by IgE-independent **MHC**-restricted T cell **peptide** epitopes.
AUTHOR(S): Haselden, B. M. (1); **LarchE, M. (1)**; Ying, S. (1); Meng, Q. (1); Dworski, R.; Kaplan, A. P.; Ferrer, M.; Shirley, K. (1); Syrigou, E. (1); Robinson, D. S. (1); **Kay, A. B. (1)**
CORPORATE SOURCE: (1) Allergy and Clinical Immunology, National Health and Lung Institute, Imperial College School of Medicine, London UK
SOURCE: Journal of Allergy and Clinical Immunology., (Jan., 2000) Vol. 105, No. 1 part 2, pp. S281.
Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000 American Academy of Allergy, Asthma and Immunology
. ISSN: 0091-6749.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Mechanisms of the late asthmatic reaction induced by IgE-independent **MHC**-restricted T cell **peptide** epitopes.
AU Haselden, B. M (1); **LarchE, M. (1)**; Ying, S. (1); Meng, Q. (1); Dworski, R.; Kaplan A. P.; Ferrer, M.; Shirley, K. (1); Syrigou, E. (1); Robinson, D. S (1) **Kay, A. B. (1)**
IT . . .
respiratory system disease
IT Chemicals & Biochemicals
BB1; CD25; CD3; CD4; CD68; CD8; IL-10 [interleukin-10]; IL 12 [interleukin-12] RFD1; T cell **peptide** epitopes: IgE independent, **MHC** restricted; cat dander: **allergen**; histamine: release; leukotrienes; neutrophil elastase; prostaglandins; tryptase
IT Alternate Indexing
Asthma (MeSH)

L5 ANSWER 5 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000121017 EMBASE
TITLE: **Peptide**-mediated immune responses in specific immunotherapy.
AUTHOR: Haselden B.M.; **Kay A.B.**; **Larche M.**
CORPORATE SOURCE: Dr. M. Larche, Allergy and Clinical Immunology, Imperial College School of Medicine, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, United Kingdom. m.larche@ic.ac.uk
SOURCE: International Archives of Allergy and Immunology, 2000 122/4 (229-237).
Refs 69
ISSN 1018 2438 CODEN: IAAIEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: [illegible]

[illegible]

[illegible] shown [illegible] an effective [illegible] disease modifying treatment [illegible] selected patients with allergic [illegible] asthma and bee and wasp venom hypersensitivity. However this form of therapy is associated with the risk of systemic anaphylaxis, which, when severe can be life threatening. A potentially significant reduction in the incidence of IgE mediated events during immunotherapy may be achieved by the use of short **peptides** corresponding to T cell epitopes which, by virtue of their size are incapable of cross linking **allergen** specific [illegible] **peptide** [illegible] employing shorter **peptides** [illegible] suggest that improved efficacy may be achieved by using **peptides** of defined major histocompatibility complex binding specificity administered in an incremental dose fashion comparable to conventional immunotherapy. This review will discuss the concept of **peptide** immunotherapy and the implications of recent studies. Copyright (C) 2000 S. Karger AG, Basel.

TI **Peptide** mediated immune responses in specific immunotherapy.
AU Haselden B.M.; **Kay A.B.**; **Larche M.**
AB Conventional immunotherapy using whole **allergen** extracts has been shown to be an effective, disease modifying treatment in carefully selected patients with allergic conjunctivo rhinitis, asthma and bee. . . A potentially significant reduction in the incidence of IgE mediated events during immunotherapy may be achieved by the use of short **peptides** corresponding to T cell epitopes which, by virtue of their size, are incapable of cross linking **allergen** specific IgE bound to the surface of mast cells and basophils. Initial clinical studies have demonstrated degrees of efficacy which have, in some cases, been associated with adverse events occurring immediately or several hours after **peptide** administration. Preliminary data from studies employing shorter **peptides** (20 amino acids or less) suggest that improved efficacy may be achieved by using **peptides** of defined major histocompatibility complex binding specificity administered in an incremental dose fashion comparable to conventional immunotherapy. This review will discuss the concept of **peptide** immunotherapy and the implications of recent studies. Copyright (C) 2000 S. Karger AG, Basel.
CT Medical Descriptors:
*allergy: . . . . histocompatibility complex
antigen recognition
helper cell
T lymphocyte activation
allergic reaction: DT, drug therapy
allergic reaction: SI, side effect
drug safety
drug efficacy
drug mechanism
immunomodulation
immunological tolerance
human
nonhuman
clinical trial
review
priority journal
***synthetic peptide: AE, adverse drug reaction**
***synthetic peptide: CT, clinical trial**
***synthetic peptide: DO, drug dose**
***synthetic peptide: DT, drug therapy**
***synthetic peptide: PD, pharmacology**
***synthetic peptide: DL, intradermal drug administration**
***synthetic peptide: NA, intranasal drug administration**
***synthetic peptide: PO, oral drug administration**
***synthetic peptide: SC, subcutaneous drug administration**
epitope
HLA antigen
allergen
adrenalin: DT, drug therapy

L5 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER:	2000:787009 CAPLUS
DOCUMENT NUMBER:	135:18478
TITLE:	**MHC**-restricted, IgE-independent, **allergen peptide** induced late asthmatic reactions
AUTHOR(S):	**Larche, Mark**
CORPORATE SOURCE:	Allergy and Clinical Immunology National Heart and Lung Institute, Imperial College School of Medicine, London, UK
SOURCE:	Chemical Immunology (2000), 78(Immunological Mechanisms in Asthma and Allergic Diseases), 30 38 CODEN: CHMIEP; ISSN: 1015-0145
PUBLISHER	S. Karger AG
DOCUMENT TYPE:	Journal
LANGUAGE	English

AB The early asthmatic reaction (EAR) is rapid and dependent upon IgE mediated release of mast cell derived mediators such as histamine and leukotrienes. Degranulation of mast cells occurs following the crosslinking of **allergen** specific IgE mols. bound to the surface of mast cells via IgE receptors. In contrast, the late asthmatic reaction (LAR) is characterized by a progressive redn. in lung function. Intradermal administration of short overlapping **peptides** derived from chain 1 of the cat **allergen** FC1P, which did not cross link IgE, elicited isolated LARs with no visible early or late response in 9 out of 40 cat allergic asthmatics. LARs were **MHC** restricted. Four of the 9 were **HLA**-DR13+ as compared with only 1 of 31 nonreactors. The other 5 reactors expressed either DR1 or DR4. To confirm **MHC** restriction, fibroblast cell lines (FCLs) transfected with **HLA**-DR mols. were used to present FC1P **peptides** to cat **allergen** specific T cell lines derived from subjects prior to **peptide** injection. FC1P3 was recognized in the context of DRB1*1301/1302 and induced specific T cell activation. T cells from a DR1+ responder proliferated and produced IL 5 in the presence of FC1P3 and DRB1*0101 FCLs whereas T cells from a DR4+ subject recognized FC1P2 when presented by DRB1*0405. Thus, short **allergen** derived **peptides** can directly initiate an **MHC** restricted, T cell dependent LAR without the requirement for an early IgE/mast cell-dependent response, in sensitized asthmatic subjects. Furthermore [illegible] **peptide** [illegible]

[illegible] allergen
peptide induced late asthmatic reactions
Larche, Mark
AB The early asthmatic reaction (EAR) is rapid and dependent upon IgE mediated release of mast cell derived mediators such as histamine and leukotrienes. Degranulation of mast cells occurs following the crosslinking of **allergen** specific IgE mols. bound to the surface of mast cells via IgE receptors. In contrast, the late asthmatic reaction (LAR) is characterized by a progressive redn. in lung function [illegible] **peptides** [illegible] **allergen** [illegible] LARs [illegible] **MHC** [illegible] **HLA** [illegible] nonreactors. The other 5 reactors expressed either DR1 or DR4 [illegible] confirm **MHC** restriction, fibroblast cell lines (FCLs) transfected with **HLA** DR mols. were used to present FC1P **peptides** to cat **allergen** specific T cell lines derived from subjects prior to **peptide** injection. FC1P3 was recognized

in the context of DRB1*1301/1302 and induced specific T cell activation. T cells from a DR1+ responder proliferated and produced IL 5 in the presence of FC1P3 and DRB1*0101 FCLs, whereas T cells from a DR4+ subject recognized FC1P2 when presented by DRB1*0405. Thus, short **allergen** derived **peptides** can directly initiate an **MHC**-restricted, T cell-dependent LAR, without the requirement for an early IgE/mast cell dependent response, in sensitized asthmatic subjects. Furthermore, re-administration of **peptide** was accompanied by a markedly reduced or abrogated lung response suggesting that T-cell hyporesponsiveness was induced following the initial LAR.

ST **MHC** IgE **allergen peptide** late asthma

IT **Allergens**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(FC1P, **MHC**-restricted, IgE independent, **allergen peptide** induced late response in cat allergic asthmatics)

IT Histocompatibility antigens
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**HLA**-DR; **MHC** restricted, IgE independent, **allergen peptide**-induced late response in cat allergic asthmatics)

IT Asthma
Cat (Felis catus)
(**MHC** restricted, IgE-independent, **allergen peptide**-induced late response in cat-allergic asthmatics)

IT **Peptides**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**MHC**-restricted, IgE independent, **allergen peptide**-induced late response in cat allergic asthmatics)

IT Interleukin 5
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**MHC** restricted, IgE-independent, **allergen peptide**-induced late response in cat-allergic asthmatics)

IT T cell (lymphocyte)
(activation; **MHC**-restricted, IgE-independent, **allergen peptide**-induced late response in cat-allergic asthmatics)

L5 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:449393 CAPLUS
DOCUMENT NUMBER: 131:86873
TITLE: Methods and compositions for desensitization
INVENTOR(S): **Larche, Mark; Kay, Anthony Barrington**
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934826	A1	19990715	WO 1999-GB80	19990111
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2317724	AA	19990715	CA 1999-2317724	19990111
AU 9920648	A1	19990726	AU 1999-20648	19990111
EP 1044019	A1	20001018	EP 1999-901014	19990111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
GB 2348808	A1	20001018	GB 2000-16438	19990111
JP 2002500198	T2	20020108	JP 2000-527273	19990111

PRIORITY APPLN. INFO.:

GB 1998-445	A	19980109
GB 1998-20474	A	19980921
WO 1999-GB80	W	19990111

AB A method of desensitizing a patient to a polypeptide **allergen** the method comprising administering to the patient a **peptide** derived from the **allergen** wherein restriction to a **MHC** Class II mol. possessed by the patient can be demonstrated by the **peptide** and the **peptide** is able to induce a late phase response in an individual who possesses the said **MHC** Class II mol. A compn. comprising a plurality of **peptides** derived from a polypeptide **allergen** wherein for at least one of the **peptides** in the compn. restriction to a **MHC** Class II mol. can be demonstrated, and the compn. is able to induce a late phase response in an individual possessing the given **MHC** Class II mol. The invention also relates to a method of selecting a **peptide** for use as an immunotherapeutic agent for desensitizing a patient to a polypeptide **allergen** capable of eliciting an allergic response in the patient [illegible] **MHC** [illegible]
[illegible] **peptide** [illegible]
[illegible] **MHC** [illegible]
[illegible] **peptide** [illegible]
[illegible] possesses the said **MHC** Class [illegible]

REFERENCE [illegible] THERE ARE [illegible] REFERENCES AVAILABLE [illegible] RECORD. ALL [illegible] AVAILABLE IN THE [illegible] FORMAT

IN **Larche, Mark; Kay, Anthony Barrington**

AB A method of desensitizing a patient to a polypeptide **allergen** the method comprising administering to the patient a **peptide** derived from the **allergen** wherein restriction to a **MHC** Class II mol. possessed by the patient can be demonstrated [illegible] **peptide** [illegible] **peptide** [illegible] **MHC** [illegible] **peptides** [illegible] **allergen** [illegible] **peptides** [illegible] **MHC** [illegible] mol. can be demonstrated, and the compn. is able to induce a late phase response in an individual possessing the given **MHC** Class II mol. The invention also relates to a method of selecting a **peptide** for use as an immunotherapeutic agent for desensitizing a patient to a polypeptide **allergen** capable of eliciting an allergic response

in the patient, which patient possesses a particular **MHC** Class II mol., the method comprising the steps of (1) selecting a candidate **peptide** derived from the polypeptide **allergen**, (2) detg. whether the candidate **peptide** demonstrates restriction to the said **MHC** Class II mol., and (3) detg. whether the candidate **peptide** is able to induce a late phase response in an individual who possesses the said **MHC** Class II mol.

ST Fel d I **allergen** allergy desensitization; immunotherapy
MHC II **allergen peptide** desensitization

IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der f I (Dermatophagoides farinae, I); compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der f II (Dermatophagoides farinae, II); compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der p I (Dermatophagoides pteronyssinus, I); compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der p II (Dermatophagoides pteronyssinus, II); compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fel d I (Felis domesticus, I); compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DP; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DQ; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA** DR2; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DR3; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DR4; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DR7; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**HLA**-DR; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**MHC** (major histocompatibility complex) class II; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Bioassay
(T cell proliferation; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Cell proliferation
(T cell, bioassay; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Worm
(**allergen** of meal worm; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization

IT Bee
Beetle (Coleoptera)
Blattaria
Calliphora vicina
Calliphoridae
Cat (Felis catus)
[illegible]
[illegible]
Grass (plant)
Guinea pig (Cavia porcellus)
Honeybee
Horse (Equus caballus)
Housefly (Musca domestica)
Mammal (Mammalia)
[illegible]
[illegible]
[illegible]
[illegible]
[illegible]
Rabbit
Ragweed (Ambrosia)
Rat
Sheep
Silkworm

Spider
Swine
Tree
Weed
Weevil
(**allergen**; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT Tenebrio molitor
(beetle **allergen**; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT Allergy
Drug delivery systems
Immunotherapy
Protein sequences
(compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT **Allergens**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT Cochliomyia hominivorax
(fly **allergen**; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT T cell (lymphocyte)
(proliferation, bioassay; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT Fly (Diptera)
(screw worm; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT Insect (Insecta)
(stinging, **allergen**; compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)
IT 136796-93-5, 23-92-Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced) 185812-53-7 197169-94-1 197170-00-6 197170-01-7 197170-07-3 197170-23-3 197170-34-6 197170-36-8 229020-52-4 229020-53-5 229020-54-6 229020-55-7 229020-56-8 229020-57-9 229020-58-0 229020-59-1 229173-24-4
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising Fel d I **allergen** epitope **peptides** for desensitization)

L5 ANSWER 8 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999307274 MEDLINE
DOCUMENT NUMBER 99307274 PubMed ID: 10377184
TITLE: Immunoglobulin E independent major histocompatibility complex restricted T cell **peptide** epitope induced late asthmatic reactions.
AUTHOR: Haselden B M; **Kay A B**; **Larche M**
CORPORATE SOURCE: Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London SW3 6LY, United Kingdom.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Jun 21) 189 (12) 1885-94
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: CLINICAL TRIAL; Journal, Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 20000728
Entered Medline: 19990726
AB Intradermal administration of short overlapping **peptides** derived from chain 1 of the cat **allergen** Fel d 1 (FC1P, that did not cross-link IgE, elicited isolated late asthmatic reactions with no visible early or late cutaneous response in 9/40 cat allergic asthmatics. Four of the nine were human histocompatibility leukocyte antigen DR13 positive, as compared with only 1/31 nonreactors. The other five reactors expressed either DR1 or DR4. To confirm major histocompatibility complex restriction, fibroblast cell lines transfected with **HLA** DR molecules were used to present FC1Ps to cat **allergen** specific T cell lines derived from subjects before **peptide** injection. FC1P3 (**peptide** 26-44 of Fel d 1 chain 1) was recognized in the context of DR13 alleles (DRB1*1301, 1302) and induced specific T cell proliferation and IL-5 production. T cells from a DR1+ responder proliferated and produced IL-5 in the presence of FC1P3 and DR1 (DRB1*0101) fibroblast cell lines, whereas T cells from a DR4+ subject recognized FC1P2 (**peptide** 22-37) when presented by DRB1*0405. We conclude that short, **allergen** derived **peptides** can directly initiate a major histocompatibility complex restricted, T cell dependent late asthmatic reaction, without the requirement for an early IgE/mast cell dependent response, in sensitized asthmatic subjects.
TI Immunoglobulin E independent major histocompatibility complex restricted T cell **peptide** epitope induced late asthmatic reactions.
AU Haselden B M; **Kay A B**; **Larche M**
AB Intradermal administration of short overlapping **peptides** derived

HLA

peptide

peptide

and DR1 (DRB1*0101) fibroblast cell lines, whereas T cells from a DR4+ subject recognized FC1P2 (**peptide** 22-37) when presented by DRB1*0405. We conclude that short, **allergen** derived **peptides** can directly initiate a major histocompatibility

*Allergens: AD, administration & dosage
Asthma: ET, etiology
*Asthma: IM, immunology
Basophils: IM, immunology
Cats
*Glycoproteins: AD, administration & dosage

HLA-DR Antigens: AN, analysis
Histamine: IM, immunology
*Immunoglobulin E: IM, immunology
Injections, Intradermal
*Major Histocompatibility Complex: IM, immunology
Middle Age
Molecular Sequence Data
Peptide Fragments: IM, immunology
*T-Lymphocytes: IM, immunology
Tuberculin IM, immunology
CN 0 (**Allergens**); 0 (Glycoproteins ; 0 (**HLA** DR Antigens ;
0 (**Peptide** Fragments); 0 (Tuberculin); 0 (**allergen** Fel
d I)

L5 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER 1999:134427 BIOSIS
DOCUMENT NUMBER: PREV199900134427
TITLE: **Peptide**-induced late asthmatic reactions following **MHC** restricted T cell activation in vivo.
AUTHOR(S): **Larche, M.**; Haselden B. M.; **Kay, A. B.**
CORPORATE SOURCE Natl. Heart Lung Inst., Imperial Coll. Sch. Med., London UK
SOURCE: Journal of Allergy and Clinical Immunology, (Jan., 1999) Vol. 103, No. 1 PART 2, pp. S204.
Meeting Info.: 55th Annual Meeting of the American Academy of Allergy, Asthma and Immunology Orlando, Florida, USA February 26-March 3, 1999 American Academy of Allergy, Asthma, and Immunology
. ISSN: 0091-6749.
DOCUMENT TYPE Conference
LANGUAGE: English
TI **Peptide**-induced late asthmatic reactions following **MHC** -restricted T cell activation in vivo.
AU **Larche, M.**; Haselden, B. M.; **Kay, A. B.**
IT . . .
and Molecular Biophysics, Immune System (Chemical Coordination and Homeostasis); Respiratory System (Respiration)
IT Parts, Structures, & Systems of Organisms
T-cell: **MHC**-restricted activation, blood and lymphatics, immune system
IT Diseases
allergic asthma: immune system disease, respiratory system disease
IT Chemicals & Biochemicals
Fel d 1: **allergen**; **HLA**; **MHC** [major histocompatibility complex]
IT Miscellaneous Descriptors
late asthmatic reactions **peptide**-induced: Meeting Abstract; Meeting Poster

L5 ANSWER 10 OF 10 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 94305369 MEDLINE
DOCUMENT NUMBER: 94305369 PubMed ID: 8032232
TITLE: Immunological events underlying the induction of T cell non-responsiveness.
AUTHOR: **Larche M**; Hoyne G; Lake R; Lamb J R
CORPORATE SOURCE: Department of Immunology, St. Mary's Hospital Medical School, Imperial College of Science, Technology and Medicine, London, UK.
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1994 Jul) 104 (3) 211-5. Ref: 43
Journal code: 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940825
Last Updated on STN: 19970203
Entered Medline: 19940815
AB T lymphocytes recognise antigen in the form of short **peptides** complexed with the class I and II products of the Major Histocompatibility Complex (**MHC**). Cellular activation follows T cell recognition of **peptide MHC** complexes at immunogenic cell surface concentrations together with the participation of the appropriate costimulatory signals. Interaction of TCRs and **peptide MHC** complexes under inappropriate conditions may result in antigen-specific non-responsiveness, commonly referred to as anergy. Here we review some recent model systems which have been employed to study the phenomenon of anergy and the use of **peptides** to induce antigen specific non-responsiveness both in vitro and in vivo.
AU **Larche M**; Hoyne G; Lake R; Lamb J R
AB T lymphocytes recognise antigen in the form of short **peptides** complexed with the class I and II products of the Major Histocompatibility Complex (**MHC**). Cellular activation follows T cell recognition of **peptide MHC** complexes at immunogenic cell surface concentrations together with the participation of the appropriate costimulatory signals. Interaction of TCRs and **peptide** MHC [illegible] peptides

Allergens: IM, immunology
[illegible]
Immunodominant Epitopes: IM [illegible]
*Lymphocyte Transformation: IM [illegible]
Mites: IM, immunology
Models, Biological
Peptides: IM, immunology
Signal Transduction: IM [illegible]
[illegible]
Allergens [illegible] Allergens [illegible] peptides

[illegible] IN 3 IN 3
L4 914 FEL IN 2 IN 2

[illegible] s l6 F peptide?
L7 125 L6 P PEPTIDE?

=>

=> s l7 and DR?
   3 FILES SEARCHED...
L8   45 L7 AND DR?

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9   24 DUP REM L8 (21 DUPLICATES REMOVED)

=> dis l9 1 24 ibib abs kwic

L9   ANSWER 1 OF 24   MEDLINE   DUPLICATE 1
ACCESSION NUMBER: 2002371605   MEDLINE
DOCUMENT NUMBER: 22110877   PubMed ID: 12114041
TITLE: Effect of T-cell **peptides** derived from
                     Fel d 1 on allergic reactions and
                     cytokine production in patients sensitive to cats: a
                     randomised controlled trial
AUTHOR: Oldfield W L G; Larche M; Kay A B
CORPORATE SOURCE: Department of Allergy and Clinical Immunology, Faculty of
                     Medicine, Imperial College, National Heart and Lung
                     Institute, London SW3 6LY, UK.
SOURCE: LANCET, (2002 Jul 6) 360 (9326) 47-53.
                     Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020716
                     Last Updated on STN: 20020724
                     Entered Medline: 20020723

AB   BACKGROUND: Some patients with asthma who are allergic to cats and are
injected intradermally with short, overlapping, T-cell **peptides**
derived from **Fel d** 1 develop late asthmatic reactions
to the **peptides**, which are associated with a reduction in
late-phase skin reactions induced by whole allergens and bronchial
hyporesponsiveness to the **peptides** on the second injection. We
aimed to ascertain the effect of multiple injections on the magnitude of
the early and late phase skin reactions to intact allergens. METHODS:
After a 9-week run-in period, we randomly assigned patients with asthma
and allergies to cats to receive either **Fel d** 1
peptides (90 microg in increasing divided doses) or placebo. The
primary outcome was late-phase cutaneous reactions to whole cat dander.
Outcomes were measured at baseline, 4-8 weeks, and 3-9 months. Analysis
was by intention to treat. FINDINGS: 16 patients were randomly assigned to
the **peptides**, and eight to placebo. All patients completed the
course of injections. Four of the 16 patients on **Fel d**
1 **peptides** had initial late asthmatic reactions, but could be
desensitised to the higher dose of **peptide**. Patients in the
peptide group but not the placebo group had a significant
reduction in the size of their late reaction to whole cat dander between
baseline and both follow-ups, but the difference between groups was not
significant (first follow-up, difference -422.8 mm(2) [95% CI -1115.0 to
269.4], p=0.43; second follow-up -1180.8 mm(2) [-2216.8 to -144.8],
p=0.058). The size of the late reaction to **Fel d** 1
significantly differed between treatment groups at both follow-ups. At
second follow-up, the size of the early reaction to **Fel**
D 1, but not to whole cat dander was significantly reduced in
those on **peptides** compared with those on placebo. The
concentration of interferon gamma and of interleukin 4 and 13, and the
amount of proliferation, significantly decreased between baseline and
second follow-up, and the concentration of interleukin 10 was
significantly higher in patients on **peptides**, however, none of
these values differed significantly between groups. Patients on
peptides had a significantly greater decrease in the concentration
of interferon gamma and interleukin 13, and in the amount of proliferation
between baseline and first follow-up than did those on placebo.
INTERPRETATION: Several, short, overlapping **Fel d** 1
T cell **peptides** have potential in treatment of cat allergy.

TI   Effect of T cell **peptides** derived from **Fel d**
1 on allergic reactions and cytokine production in patients sensitive to
cats: a randomised controlled trial.

AB   BACKGROUND: Some patients with asthma who are allergic to cats and are
injected intradermally with short, overlapping, T-cell **peptides**
derived from **Fel d** 1 develop late asthmatic reactions
to the **peptides**, which are associated with a reduction in
late phase skin reactions induced by whole allergens and bronchial
hyporesponsiveness to the **peptides** on the second injection. We
aimed to ascertain the effect of multiple injections on the magnitude of
the early and. . . . allergens. METHODS: After a 9 week run in period, we
randomly assigned patients with asthma and allergies to cats to receive
either **Fel d** 1 **peptides** (90 microg in
increasing divided doses) or placebo. The primary outcome was late phase
cutaneous reactions to whole cat dander. Outcomes. . . . baseline, 4-8
weeks, and 3-9 months. Analysis [illegible]

[illegible] **Fel** [illegible] **peptides**
[illegible]
[illegible] **peptide** [illegible] **peptide**
[illegible] placebo group had a significant [illegible]
[illegible]
[illegible]
late reaction to **Fel d** 1 significantly differed
between treatment groups at both follow ups. At second follow up, the size
of the early reaction to **Fel D** 1, but not to whole cat
dander was significantly reduced in those on **peptides** compared
with those on placebo. The concentration of interferon gamma and [illegible]
[illegible]
peptides [illegible]
between groups. Patients on **peptides** [illegible]
decrease in the concentration of interferon gamma and interleukin [illegible]
in the amount of proliferation between baseline and first follow up than
did those on placebo. INTERPRETATION: Several, short, overlapping
Fel d 1 T cell **peptides** have potential in
treatment of cat allergy.

CT Check Tags: Animal; Female; Human; Male; Support, Non U.S. Gov't
Adult
Allergens: AE, adverse effects
*Allergens: TU, therapeutic use
***Asthma: DT, drug therapy**
Cats
*Cytokines: BI, biosynthesis
***Hypersensitivity: DT, drug therapy**
Injections, Intradermal
Middle Age
Peptides: TU, therapeutic use
Treatment Outcome

L9 ANSWER 2 OF 24 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001420419 MEDLINE
DOCUMENT NUMBER: 21361316 PubMed ID: 11468000
TITLE: Allergenic proteins are fragmented in low concentrations of sodium hypochlorite.
AUTHOR: Chen P; Eggleston P A
CORPORATE SOURCE: Johns Hopkins University, 600 North Wolfe Street, Baltimore, MD 21287, USA.
CONTRACT NUMBER: ES07527 (NIEHS)
ES09601 (NIEHS)
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (2001 Jul) 31 (7) 1086-93.
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20010924
Entered Medline: 20010920

AB BACKGROUND: To facilitate allergen removal from indoor environments, it would be helpful to have household cleaning products that modified allergenic activity. Because NaOCl dissolves proteins in high concentrations and is both capable of killing bacteria and viruses and inactivating viral antigens at somewhat lower concentrations, we explored its effects on Mus m 1 and other indoor allergens. OBJECTIVE: To examine the ability of NaOCl to reduce the allergenicity of Mus m 1 and other indoor allergens. METHODS: Using purified mouse urinary allergen, we examined the effect on protein measured by Coomassie protein assay and on Mus m 1 measured by ELISA. We also examined the effects using SDS/PAGE and Western blots probed with sheep anti-Mus m 1 and with allergic human serum. RESULTS: When NaOCl and Mus m 1 were combined in a molar ratio of 100 : 1, IgE binding to Mus m 1 on Western blot was significantly reduced. At higher NaOCl concentrations the protein appeared to fragment and eventually became undetectable. Fragmentation appeared to be random in that **peptides** of a wide range of apparent molecular weight were produced. The reaction was complete within 1-2 min at OCl : pr ratios of greater than 200 : 1 and was optimal at pH 7.4. Immunological activity of other allergens (**Fel d** 1, Bla g 1, Der p 1) was decreased in vitro and **dried** allergen extracts were removed from surfaces. Adding an extraneous protein, BSA, to NaOCl:Mus m 1 solutions decreased the effect of NaOCl on the allergen. CONCLUSIONS: We concluded that NaOCl at concentrations commonly used in household products is capable of **dramatically** affecting allergenic protein.

AB . . . At higher NaOCl concentrations the protein appeared to fragment and eventually became undetectable. Fragmentation appeared to be random in that **peptides** of a wide range of apparent molecular weight were produced. The reaction was complete within 1-2 min at OCl : pr ratios of greater than 200 : 1 and was optimal at pH 7.4. Immunological activity of other allergens (**Fel d** 1, Bla g 1, Der p 1) was decreased in vitro and **dried** allergen extracts were removed from surfaces. Adding an extraneous protein, BSA, to NaOCl:Mus m 1 solutions decreased the effect of NaOCl on the allergen. CONCLUSIONS: We concluded that NaOCl at concentrations commonly used in household products is capable of **dramatically** affecting allergenic protein.

L9 ANSWER 3 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001331879 EMBASE
TITLE: Asthma, rhinitis, other respiratory diseases: Proliferation and release of IL-5 and IFN-.gamma. by peripheral blood mononuclear cells from cat-allergic asthmatics and rhinitics, non-cat-allergic asthmatics, and normal controls to **peptides** derived from **Fel d** 1 chain 1.
AUTHOR: Haselden B.M.; Syrigou E.; Jones M.; Huston D.; Ichikawa K.; Chapman M.D.; Kay A.B.; Larche M.
CORPORATE SOURCE: Dr. M. Larche, Deptartment of Allergy, National Heart and Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, United Kingdom
SOURCE: Journal of Allergy and Clinical Immunology, (2001) 108/3 (349-356).
Refs: 37
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: [illegible]

[illegible]

AB [illegible] was to determine differences in T-cell recognition of epitopes within allergenic sequences, in terms of proliferation and cytokine production in subjects with atopic asthma compared with subjects with allergic rhinitis and normal controls. Methods: Proliferative responses and IL-5/IFN-.gamma. release patterns from PBMCs from cat-allergic asthmat[illegible] **peptides** [illegible] **Fel d** [illegible] differ with respect [illegible] **Fel d** 1 **peptides**. In all groups the IFN-.gamma. responses were predominantly to the amino-terminus **peptides**. Cat-allergic and non-cat-allergic asthmatic subjects (and not cat-allergic rhinitic subjects and normal controls) made IL-5 responses to most of the **Fel d** 1 **peptides**.

the result being a mixed (T H 0) cytokine response at the N terminus and a restricted (T H 2) response at the C terminus. Conclusion: Proliferative and IL 5/IFN-.gamma. responses of T cells from asthmatic and atopic rhinitic subjects and normal controls to allergen **peptides** can be dissociated. Furthermore, differing cytokine responses to **peptides** derived from a single antigen suggest that certain domains of the molecule might preferentially induce IL 5 rather than IFN .gamma. and as a result could be more important in disease pathogenesis.

TI . . . of IL-5 and IFN .gamma. by peripheral blood mononuclear cells from cat allergic asthmatics and rhinitics, non cat allergic asthmatics, and normal controls to **peptides** derived from **Fel d** 1 chain 1.

AB . . . rhinitic, and non cat allergic asthmatic subjects and nonatopic normal controls were determined in primary cultures. Cells were challenged with 7 overlapping **peptides** spanning chain 1 of the major cat allergen, **Fel d** I. Results: The 4 groups did not differ with respect to the ability to mount proliferative responses to **Fel d** 1 **peptides**. In all groups, the IFN-.gamma. responses were predominantly to the amino terminus **peptides**. Cat-allergic and non cat allergic asthmatic subjects (and not cat-allergic rhinitic subjects and normal controls) made IL 5 responses to most of the **Fel d** I **peptides**, the result being a mixed (T(H)0) cytokine response at the N terminus and a restricted (T(H)2) response at the C terminus. Conclusion: Proliferative and IL-5/IFN .gamma. responses of T cells from asthmatic and atopic rhinitic subjects and normal controls to allergen **peptides** can be dissociated. Furthermore, differing cytokine responses to **peptides** derived from a single antigen suggest that certain domains of the molecule might preferentially induce IL-5 rather than IFN-.gamma. and. . .

CT Medical Descriptors:
*allergic . . . study
human cell
adult
article
priority journal
*interleukin 5: EC, endogenous compound
*gamma interferon: EC, endogenous compound
*peptide: EC, endogenous compound
epitope: EC, endogenous compound
allergen
fel d 1 allergen
unclassified drug

L9 ANSWER 4 OF 24 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001262386 MEDLINE
DOCUMENT NUMBER: 21203301 PubMed ID: 11306988
TITLE: Mechanisms of T cell peptide epitope-dependent late asthmatic reactions
AUTHOR: Larche M; Haselden B M; Oldfield W L; Shirley K; North J; Meng Q; Robinson D S; Ying S; Kay A B
CORPORATE SOURCE: Allergy and Clinical Immunology, Imperial College School of Medicine, London, UK.. m.larche@ic.ac.uk
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 272-5.
Journal code: 9211652. ISSN: 1018-2438.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Short **peptide** sequences corresponding to T cell epitopes have been identified in the major cat allergen **Fel d** 1. In order to directly activate allergen specific T cells in cat allergic asthmatic individuals, **peptides** were administered by intradermal injection. Subsequently, a proportion of subjects experienced a delayed reduction of airway calibre manifested as a decrease in FEV 1. Changes in lung function occurred approximately 3 h after **peptide** injection, peaked at 6 h and resembled an isolated late asthmatic reaction (LAR). Using molecular tissue typing techniques, it was determined that many of the individuals experiencing isolated LAR expressed particular HLA **DR** molecules. These molecules were shown in subsequent experiments to bind individual **peptides** within the preparation and thus to activate T cells in a major histocompatibility complex (MHC)-restricted fashion. The precise mechanisms whereby MHC restricted activation of allergen specific T cells gives rise to bronchoconstriction are currently under investigation.
Copyright 2001 S. Karger AG, Basel

AB Short **peptide** sequences corresponding to T cell epitopes have been identified in the major cat allergen **Fel d** 1. In order to directly activate allergen specific T cells in cat allergic asthmatic individuals, **peptides** were administered by intradermal injection. Subsequently, a proportion of subjects experienced a delayed reduction of airway calibre manifested as a decrease in FEV 1. Changes in lung function occurred approximately 3 h after **peptide**

[illegible] peptides

[illegible]
*Asthma: IM, immunology
Cats
Cell Line
*Epitopes: IM, immunology
Forced Expiratory Volume
[illegible]
HLA-DR Antigens: IM, immunology
[illegible]
[illegible]
[illegible]
[illegible]
Epitopes; Glycoproteins; HLA DR Antigens
Peptides; allergen Fel d 1

L9 ANSWER 5 OF 24 EMBASE COPYRIGHT [illegible]
ACCESSION NUMBER: 2001142844 EMBASE

TITLE: Detection of Fel d 1 immunoglobulin G immune complexes in cord blood and sera from allergic and non allergic mothers.
AUTHOR: Casas R.; Bjorksten B.
CORPORATE SOURCE: R. Casas, Department of Health and Environment, Division of Paediatrics, Linkoping University Hospital, S 581 85 Linkoping, Sweden. rosaura.casas@kfc.liu.se
SOURCE Pediatric Allergy and Immunology, (2001) 12/2 (59-64).
Refs: 22
ISSN: 0905 6157 CODEN: PALUEE
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB It is an established fact that T-cell responses of fetal origin to inhalant allergens are present in most cord blood samples. These immune responses could be explained by trans-placental passage of **peptides**, either as free antigens or in complexes with immunoglobulin G (IgG), providing the fetus with a trigger for priming the T cell system already present in utero. The aim of this study was to investigate the presence of the major cat allergen, **Fel d** 1, in complexes with IgG in cord blood and maternal sera. Serum samples from 75 mothers (38 allergic, 37 non-allergic), and cord blood from their infants, were investigated for the presence of **Fel d** 1-IgG immune complexes (ICs) by using an amplified enzyme-linked immunosorbent assay (ELISA). Three monoclonal antibodies to **Fel d** 1 were used for coating. The specificity of the method was confirmed by inhibition experiments. ICs of **Fel d** 1 IgG were detected in the sera of 45% allergic and 49% non-allergic mothers, and in, respectively, 34% and 41% of their infants. Therefore, neither the prevalence nor the level of ICs were affected by maternal allergy. Low levels of trans-placentally transferred ICs can provide the fetus with a signal for the priming of T-cell responses to inhalant allergens. However, this is not necessarily related to allergic disease.
AB . . . to inhalant allergens are present in most cord blood samples. These immune responses could be explained by trans placental passage of **peptides**, either as free antigens or in complexes with immunoglobulin G (IgG), providing the fetus with a trigger for priming the. . . . system already present in utero. The aim of this study was to investigate the presence of the major cat allergen, **Fel d** 1, in complexes with IgG in cord blood and maternal sera. Serum samples from 75 mothers (38 allergic, 37 non-allergic), and cord blood from their infants, were investigated for the presence of **Fel d** 1-IgG immune complexes (ICs) by using an amplified enzyme-linked immunosorbent assay (ELISA). Three monoclonal antibodies to **Fel d** 1 were used for coating. The specificity of the method was confirmed by inhibition experiments. ICs of **Fel d** 1 IgG were detected in the sera of 45% allergic and 49% non allergic mothers, and in, respectively, 34% and 41% of. . .
CT Medical Descriptors:
*allergy
T . . . . complex
fetomaternal transfusion
immune response
maternal serum
enzyme linked immunosorbent assay
human
female
clinical article
controlled study
infant
article
priority journal
*immunoglobulin G: EC, endogenous compound
*fel d 1
allergen
peptide: EC, endogenous compound
monoclonal antibody
unclassified drug

L9 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:83091 CAPLUS
DOCUMENT NUMBER: 132:136407
TITLE: Peptides of human T cell reactive feline protein TRFP
INVENTOR(S): Gefter, Malcolm L.; Garman, Richard D.; Greenstein, Julia L.; Kuo, Mei Chang; Manville, Malcolm; Brinet, Thomas J
PATENT ASSIGNEE(S): Immulogic Pharmaceutical Corp., USA
SOURCE U.S., 105 pp., Cont. in part of U.S. 5,547,669.
CODEN USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
US 6248862	A	[illegible]	[illegible]	[illegible]
US 6025162	A	20000215	US 1995 481944	19950608
US 6120769	A	20000919	US 1995 481184	19950608
FI 9504895	A	19951013	FI 1995 4895	19951013
NO 9504095	A	19951213	NO 1995 4095	19951013
FI 9603331	A	[illegible]	FI 1996 3331	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
US 1992 864719	B1	19920915		
US 1993 6116	B2	19930115		
WO 1993 US3471	W	19930414		
US 1994 300928	A3	19940902		
FI 1995 4895	A	19951013		

AB A substantially pure, covalently linked human T cell reactive feline protein (TRFP) has been isolated from vacuum bag ext. obtained by affinity purifn. of house dust collected from several homes with cats; DNA encoding all or a portion of the TRFP or peptide; compns. contg. such a protein or peptide or portions thereof; and antibodies reactive with the TRFP or peptide are disclosed. Also disclosed are recombinant TRFP or peptide; modified or mutated TRFP peptides; their use for diagnostic or therapeutic purposes.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Allergens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**Fel d** I (Felis domesticus, I), same as TRFP; **peptides** of human T cell reactive feline protein or TRFP for diagnosis and therapy of cat allergy)

IT **Drug** delivery systems
(carriers; peptides of human T cell reactive feline protein or TRFP for diagnosis and therapy of cat allergy)

IT **Drug** delivery systems
(injections; peptides of human T cell reactive feline protein or TRFP for diagnosis and therapy of cat allergy)

IT **Drug** delivery systems
(oral; peptides of human T cell reactive feline protein or TRFP for diagnosis and therapy of cat allergy)

IT 136796-89-9, 45-95-Glycoprotein TRFP (Felis catus chain 2 95 amino acid isoform protein moiety reduced) 136796-94-6 136797-19-8 136797-20-1 144996-56-5, Allergen Fel dI (Felis catus chain 2 protein moiety reduced) 149119-99-3 256500-74-0 256500-76-2 256500-79-5 256500-80-8, Allergen **Fel d** 1 (cat clone C1 chain 1) 256500-81-9 256500-82-0, Allergen **Fel d** 1 (cat clone 2 chain 2) 256500-83-1 256500-84-2 256500-85-3
RL PRP (Properties)
(amino acid sequence; **peptides** of human T cell reactive feline protein or TRFP for diagnosis and therapy of cat allergy)

L9 ANSWER 7 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001053542 EMBASE
TITLE: Antigen specific T cell tolerance down regulates mast cell responses in vivo.
AUTHOR: Treter S.; Luqman M.
CORPORATE SOURCE: S. Treter, ImmuLogic Pharmaceutical Corporation, 610 Lincoln Street, Waltham MA 02154, United States
SOURCE: Cellular Immunology, (15 Dec 2000) 206/2 (116-124).
Refs: 41
ISSN: 0008-8749 CODEN: CLIMB8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Fel d** I is the major cat allergen that induces asthma and allergic rhinitis in humans. To investigate the mechanism of allergic responses to this allergen, a mouse model was developed. Mice sensitized to chain 1 of **Fel d** I exhibited T cell responses, B cell responses, and mast cell responses when challenged with the protein. Subcutaneous injections of **peptides** containing the dominant T cell epitopes of the allergen induced T cell tolerance in presensitized mice. When challenged with the allergen intratracheally, these tolerized mice produced a decreased amount of histamine in vivo. The decrease in histamine release was not solely dependent on the reduction of allergen specific IgE. These data show that mast cell activity in mice with an ongoing sensitivity to allergen can be regulated through **peptide** induced T cell tolerance. (C)OPYRGT. 2000 Academic Press.

AB **Fel d** I is the major cat allergen that induces asthma and allergic rhinitis in humans. To investigate the mechanism of allergic responses to this allergen, a mouse model was developed. Mice sensitized to chain 1 of **Fel d** I exhibited T cell responses, B cell responses, and mast cell responses when challenged with the protein. Subcutaneous injections of **peptides** containing the dominant T cell epitopes of the allergen induced T cell tolerance in presensitized mice. When challenged with the. . IgE. These data show that mast cell activity in mice with an ongoing sensitivity to allergen can be regulated through **peptide** induced T cell tolerance. [illegible] Academic Press.

CT Medical Descriptors:
*T lymphocyte
*immunological tolerance
*mast cell
antigen specificity
asthma
allergic rhinitis
B lymphocyte
allergic reaction
nonhuman
female
mouse
animal experiment
animal model
[illegible]
[illegible]
histamine
unclassified drug

L9 ANSWER 8 OF 24 CAPLUS COPYRIGHT [illegible] ACS

ACCESSION NUMBER: 1999:449393 CAPLUS
DOCUMENT NUMBER: [illegible]
[illegible]
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934826	A1	19990715	WO 1999 GB80	19990111
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2317724	AA	19990715	CA 1999 2317724	19990111
AU 9920648	A1	19990726	AU 1999 20648	19990111
EP 1044019	A1	20001018	EP 1999 901014	19990111
R	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
GB 2348808	A1	20001018	GB 2000 16438	19990111
JP 2002500198	T2	20020108	JP 2000 527273	19990111

PRIORITY APPLN. INFO.: GB 1998-445 A 19980109
GB 1998-20474 A 19980921
WO 1999 GB80 W 19990111

AB A method of desensitizing a patient to a polypeptide allergen the method comprising administering to the patient a peptide derived from the allergen wherein restriction to a MHC Class II mol. possessed by the patient can be demonstrated by the peptide and the peptide is able to induce a late phase response in an individual who possesses the said MHC Class II mol. A compn. comprising a plurality of peptides derived from a polypeptide allergen wherein for at least one of the peptides in the compn. restriction to a MHC Class II mol. can be demonstrated, and the compn. is able to induce a late phase response in an individual possessing the given MHC Class II mol. The invention also relates to a method of selecting a peptide for use as an immunotherapeutic agent for desensitizing a patient to a polypeptide allergen capable of eliciting an allergic response in the patient, which patient possesses a particular MHC Class II mol., the method comprising the steps of (1) selecting a candidate peptide derived from the polypeptide allergen, (2) detg. whether the candidate peptide demonstrates restriction to the said MHC Class II mol., and (3) detg. whether the candidate peptide is able to induce a late phase response in an individual who possesses the said MHC Class II mol.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ST **Fel d** I allergen allergy desensitization immunotherapy MHC II allergen **peptide** desensitization

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der f I (Dermatophagoides farinae, I); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der f II (Dermatophagoides farinae, II); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der p I (Dermatophagoides pteronyssinus, I); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Der p II (Dermatophagoides pteronyssinus, II); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Fel d** I (Felis domesticus, I); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA DP; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA DQ; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HLA **DR2**; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Histocompatibility antigens

[illegible] **peptides** [illegible]

[illegible] (Biological study); PROC (Process)
HLA **DR4**; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
HLA **DR7**; compns. comprising **Fel d** I allergen epitope **peptides** for [illegible]

[illegible] HLA DR [illegible] **Fel d** I allergen epitope **peptides** for desensitization

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
MHC (major histocompatibility complex Class II); compns. comprising **Fel d** I allergen epitope **peptides** for

desensitization

IT Bioassay
(T cell proliferation; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Cell proliferation
(T cell, bioassay; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Worm
(allergen of meal worm; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Bee
Beetle (Coleoptera)
Blattaria
Calliphora vicina
Calliphoridae
Cat (Felis catus)
Cattle
Chironomidae
Dog (Canis familiaris)
Food
Fruit fly
Fungi
Gerbil
Grass (Poaceae)
Guinea pig (Cavia porcellus)
Honeybee
Horse (Equus caballus)
Housefly (Musca domestica)
Mammal (Mammalia)
Mite and Tick
Mold (fungus)
Moth
Mouse
Pollen
Rabbit
Ragweed (Ambrosia)
Rat
Sheep
Silkworm
Spider
Swine
Tree
Weed
Weevil
(allergen; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Tenebrio molitor
(beetle allergen; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergy
Drug delivery systems
Immunotherapy
Protein sequences
(compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Cochliomyia hominivorax
(fly allergen; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT T cell (lymphocyte)
(proliferation, bioassay; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

IT Fly (Diptera)
(screw worm; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Insect (Insecta
(stinging, allergen; compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT 136796 93 5, 23-92 Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced) 185812 53 7 197169 94 1 197170 00 6 197170 01 7 197170 07 3 197170 23 3 197170 34 6 197170 36 8 229020 52 4 229020 53 5 229020 54 6 229020 55 7 229020 56 8 229020 57 9 229020 58 0 229020 59 1 229173 24 4
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising **Fel d** I allergen epitope **peptides** for desensitization)

L9 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:388060 CAPLUS
DOCUMENT NUMBER: 131:31034
TITLE: Purification and therapeutic application of peptide complexes with heat shock proteins
INVENTOR(S): Wallen, Erik S.; Moseley, Pope L.
PATENT ASSIGNEE(S): The University of New Mexico, USA
[illegible]

[illegible]

PATENT NO. [illegible] APPLICATION NO. [illegible]

WO 9929182 A1 [illegible] WO 1998-US25734 [illegible]
W: BR, CA, JP, MX
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
[illegible]

PRIORITY APPLN. INFO.: [illegible]
US 1997-986234 A 19971205
[illegible]
[illegible]
WO 1998-US25734 W 19981204

AB The authors disclose methods for synthesizing heat shock protein (hsp) **peptide** complexes. The complexes are prepd. by capturing the hsps on agarose immobilized gelatin and effecting their elution with the derived **peptide**(s). Alternatively, the heat shock proteins are captured on an affinity matrix as complexes with ADP prior to their subsequent elution with **peptide**(s). In addn., the present invention also provides a method for treating an allergic disease in which a heat shock protein antigen complex is administered to a mammal in an amt. sufficient to reduce the susceptibility of the mammal to a Th2 response for the allergic disease. In an example of desensitization, mice were pretreated with HSP70 complexes contg. **peptides** derived from the **Fel d** 1 allergen prior to antigen challenge.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The authors disclose methods for synthesizing heat shock protein (hsp) **peptide** complexes. The complexes are prepd. by capturing the hsps on agarose immobilized gelatin and effecting their elution with the derived **peptide**(s). Alternatively, the heat shock proteins are captured on an affinity matrix as complexes with ADP prior to their subsequent elution with **peptide**(s). In addn., the present invention also provides a method for treating an allergic disease in which a heat shock protein antigen complex is administered to a mammal in an amt. sufficient to reduce the susceptibility of the mammal to a Th2 response for the allergic disease. In an example of desensitization, mice were pretreated with HSP70 complexes contg. **peptides** derived from the **Fel d** 1 allergen prior to antigen challenge.

IT **Drug** delivery systems
(aerosols, inhalants; heat shock protein peptide complexes in)

IT **Drug** delivery systems
(oral; heat shock protein peptide complexes in)

IT **Drug** delivery systems
(topical; heat shock protein peptide complexes in)

L9 ANSWER 10 OF 24 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 1999307274 MEDLINE
DOCUMENT NUMBER: 99307274 PubMed ID: 10377184
TITLE: Immunoglobulin E independent major histocompatibility complex-restricted T cell peptide epitope-induced late asthmatic reactions.
AUTHOR: Haselden B M; Kay A B; Larche M
CORPORATE SOURCE: Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London SW3 6LY, United Kingdom.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Jun 21) 189 (12) 1885-94.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 20000728
Entered Medline: 19990726

AB Intradermal administration of short overlapping **peptides** derived from chain 1 of the cat allergen **Fel d** 1 (FC1P) that did not cross link IgE, elicited isolated late asthmatic reactions with no visible early or late cutaneous response in 9/40 cat-allergic asthmatics. Four of the nine were human histocompatibility leukocyte antigen **DR13**-positive, as compared with only 1/31 nonreactors. The other five reactors expressed either **DR1** or **DR4**. To confirm major histocompatibility complex restriction, fibroblast cell lines transfected with HLA-**DR** molecules were used to present FC1Ps to cat allergen specific T cell lines derived from subjects before **peptide** injection. FC1P3 (**peptide** 28-44 of **Fel d** 1 chain 1) was recognized in the context of **DR13** alleles (**DRB1***1301, 1302) and induced specific T cell proliferation and IL 5 production. T cells from a **DR1**(+) responder proliferated and produced IL 5 in the presence of FC1P3 and **DR1** (**DRB1***0101) fibroblast cell lines, whereas T cells from a **DR4**(+) subject recognized FC1P2 (**peptide** 22-37) when presented by **DRB1***0405. We conclude that short, allergen derived **peptides** can directly initiate a major histocompatibility complex restricted, T cell dependent late asthmatic reaction, without the requirement for an early IgE/mast cell dependent response, in sensitized asthmatic subjects.

AB Intradermal administration of short overlapping **peptides** derived from chain 1 of the cat allergen **Fel d** 1 (FC1P) that did not cross link IgE, elicited isolated late asthmatic reactions with no visible early or late cutaneous response in 9/40 cat allergic asthmatics. Four of the nine were human histocompatibility leukocyte antigen **DR13** positive, as compared with only 1/31 nonreactors. The other five reactors expressed either **DR1** or **DR4**. To confirm major histocompatibility complex restriction, fibroblast cell lines transfected with HLA **DR** molecules were used to present FC1Ps to cat allergen specific T cell lines derived from subjects before **peptide** injection. FC1P3 (**peptide** 28 44 of **Fel d** 1 chain 1) was recognized in the context of **DR13** alleles (**DRB1***13 [illegible]
[illegible] **DRB1*** [illegible]
DR4 [illegible] peptide [illegible]
DRB1* [illegible]
allergen derived **peptides** [illegible]
[illegible]
[illegible]

[illegible]
& dosage
Amino Acid Sequence
Asthma: [illegible]
[illegible]
HLA-DR Antigens: AN, analysis
Histamine: IM, immunology
*Immunoglobulin E: IM, immunology
Injections, Intradermal
*Major Histocompatibility Complex: IM, immunology
Middle Age

CN 0 (Allergens) ; 0 (Glycoproteins) ; 0 (HLA DR Antigens) ; 0 (Peptide Fragments) ; 0 (Tuberculin) ; 0 (allergen Fel d 1)

L9 ANSWER 11 OF 24 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 1999017350 MEDLINE
DOCUMENT NUMBER: 99017350 PubMed ID: 9802364
TITLE: Immunotherapy with **Fel d** 1 **peptides** decreases IL 4 release by peripheral blood T cells of patients allergic to cats.

AUTHOR: Pene J; Desroches A; Paradis L; Lebel B; Farce M; Nicodemus C F; Yssel H; Bousquet J
CORPORATE SOURCE: INSERM U 454, Hopital Arnaud de Villeneuve, Montpellier, France.

SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Oct) 102 (4 Pt 1) 571 8.
Journal code: 1275002. ISSN: 0091 6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981119

AB BACKGROUND: Cells producing a T(H2) cytokine profile play an important role in the onset and maintenance of atopic diseases, and therefore specific immunotherapy is aimed to induce a switch to cells producing a T(H1) or T(H0) cytokine profile. Recently, a novel form of immunotherapy making use of synthetic **peptides** from the major cat allergen **Fel d** 1 has been developed, but its mechanisms of action are unknown. OBJECTIVES: We examined the effects of immunotherapy with **Fel d** 1 **peptides** on the response to bronchial provocation tests (PD20FEV1) with a standardized **Fel d** 1 cat extract on **Fel d** 1 specific serum IgE and IgG levels and in vitro IL 4 and IFN gamma production. METHODS: Patients allergic to cats received 6 weekly injections of 7.5 micro(g) (low dose), 75 micro(g) (medium dose), or 750 micro(g) (high dose) of **Fel d** 1 **peptides** (25 patients) or a placebo (6 patients). RESULTS: Six weeks after ending immunotherapy, posttreatment PD20FEV1 was not significantly different between the treated and placebo groups. However, in the medium and high dose groups there was a significant improvement between baseline and posttreatment days. IL 4 release was significantly reduced in the high dose treated group (P <.005, Wilcoxon W test), whereas it was unchanged in the low or medium dose and in the placebo-treated groups. In all groups, IFN gamma, IgE, and IgG levels remained unchanged. CONCLUSION: There was no correlation between the improvement of PD20FEV1 and the decrease in IL 4 production. These data suggest that **peptide** immunotherapy may act by shifting the **Fel d** 1-induced response of PBMCs in vitro from the T(H2) like to the T(H0) like phenotype.

TI Immunotherapy with **Fel d** 1 **peptides** decreases IL 4 release by peripheral blood T cells of patients allergic to cats.

AB . . . a switch to cells producing a T(H1) or T(H0) cytokine profile. Recently, a novel form of immunotherapy making use of synthetic **peptides** from the major cat allergen **Fel d** 1 has been developed, but its mechanisms of action are unknown. OBJECTIVES: We examined the effects of immunotherapy with **Fel d** 1 **peptides** on the response to bronchial provocation tests (PD20FEV1) with a standardized **Fel d** 1 cat extract on **Fel d** 1 specific serum IgE and IgG levels and in vitro IL 4 and IFN gamma production. METHODS: Patients allergic to cats received 6 weekly injections of 7.5 micro(g) (low dose), 75 micro(g) (medium dose), or 750 micro(g) (high dose) of **Fel d** 1 **peptides** (25 patients) or a placebo (6 patients). RESULTS: Six weeks after ending immunotherapy, posttreatment PD20FEV1 was not significantly different between. . . . CONCLUSION: There was no correlation between the improvement of PD20FEV1 and the decrease in IL 4 production. These data suggest that **peptide** immunotherapy may act by shifting the **Fel d** 1 induced response of PBMCs in vitro from the T(H2) like to the T(H0) like phenotype.

CT . . . Animal; Female; Human; Support, Non U.S. Gov't
Adult
*Allergens: TU, therapeutic use
Basophils: ME, metabolism
Bronchial Provocation Tests
Cats
*Desensitization, Immunologic
Dose-Response Relationship, Drug
Double Blind Method
Glycoproteins: AD, administration & dosage
*Glycoproteins: TU, therapeutic use
Immunoglobulin E: BI, biosynthesis
Immunoglobulin G: . . .

. . . Lichtenstein, Lawrence M; . . . David M . . .
. . . Johns Hopkins Asthma Allergy Center . . .
Bayview Circle, Baltimore, MD . . . USA

SOURCE: Journal of Allergy and Clinical Immunology, (April, 1998) Vol. 10, No. 4 PART 1, pp. 506 513.
ISSN: 0091 6749.
DOCUMENT TYPE: Article

. . . **peptide** . . .
peptides . . .
. . . We sought to study the effect of . . . **peptide** therapy on ex vivo antigen specific T cell responses. Methods: Antigen specific T cell lines were generated from subjects enrolled in a double blind placebo controlled two dose study of the ALLERVAX CAT therapeutic containing **Fel d** 1 **peptides** (ImmuLogic Pharmaceutical Corp., Waltham, Mass. . . . and . . . respectively) for

groups receiving placebo, 75 mug, or 750 mug . Each subject had three lines propagated before and after receiving **peptide** therapy; antigens used were cat hair extract, **Fel d 1** **peptides**, and tetanus toxoid negative control . Proliferative responses and cytokine generation from each line were assessed after two restimulations with antigen and autologous antigen presenting cells. Results: The **Fel d 1 peptide** lines showed a dose dependent decrease of IL 4 production p=0.02 and 0.025, respectively, for the 750 Kg group vs both the 75 mug and placebo groups . IL 4 production from the cat hair allergen extract lines and interferon gamma production from both the **Fel d 1** **peptide** lines and cat hair allergen extract lines showed no statistically significant changes. The control tetanus toxoid lines showed no changes in cytokine production; there were no significant changes in proliferation with any of the antigens in any of the treatment groups. In the clinical arm of the trial, only the 750 mug dose of **peptides** produced a significant response. Conclusions: **Peptide** therapy induces a significant, dose dependent decrease in **peptide** stimulated IL 4 production, consistent with either a shift in T-cell phenotype or **peptide** specific T cell tolerance.

AB Background **Peptide** therapy targets T cells directly with short **peptides** containing multiple T cell receptor epitopes. Murine studies suggest T cell anergy as the mechanism of action; however, changes in T cell cytokine profiles may be more relevant in human beings. Objective: We sought to study the effects of **peptide** therapy on ex vivo antigen specific T cell responses. Methods: Antigen specific T-cell lines were generated from subjects enrolled in a double blind, placebo controlled, two dose study of the ALLERVAX CAT therapeutic, containing **Fel d 1 peptides** (ImmuLogic Pharmaceutical Corp., Waltham, Mass.) (n=7, 8, and 7, respectively, for groups receiving placebo, 75 mug, or 750 mug). Each subject had three lines propagated before and after receiving **peptide** therapy; antigens used were cat hair extract, **Fel d 1** **peptides**, and tetanus toxoid (negative control). Proliferative responses and cytokine generation from each line were assessed after two restimulations with antigen and autologous antigen presenting cells. Results: The **Fel d 1 peptide** lines showed a dose-dependent decrease of IL 4 production (p=0.02 and 0.025, respectively, for the 750 Kg group vs both the. . . 75 mug and placebo groups). IL-4 production from the cat hair allergen extract lines and interferon gamma production from both the **Fel d 1** **peptide** lines and cat hair allergen extract lines showed no statistically significant changes. The control tetanus toxoid lines showed no changes . antigens in any of the treatment groups. In the clinical arm of the trial only the 750 mug dose of **peptides** produced a significant response. Conclusions: **Peptide** therapy induces a significant, dose dependent decrease in **peptide** stimulated IL 4 production, consistent with either a shift in T-cell phenotype or **peptide** specific T cell tolerance.

IT . . .
    blood and lymphatics, immune system

IT Diseases
    cat allergy

IT Chemicals & Biochemicals
    cat hair allergen extract, interferon gamma; ALLERVAX CAT: **Fel d 1 peptide** therapy product, immunologic **drug**; **Fel d 1 peptide**, IL 4 [interleukin 4]

L9 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997 640833 CAPLUS
DOCUMENT NUMBER: 127:306603
TITLE: Cryptic peptides and method for their identification
INVENTOR(S): Kay, Anthony Barrington; Larche Mark
PATENT ASSIGNEE S: Imperial College of Science, Technology and Medicine, UK; Kay, Anthony Barrington; Larche, Mark
SOURCE: PCT Int Appl., 49 pp. CODEN PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM COUNT: 1
PATENT INFORMATION

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735193	A1	[illegible]	WO 1997 GB783	19970320
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, [illegible], KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2247009	AA	19970925	CA 1997 2247009	19970320
AU 9720365	A1	19971010	AU 1997 20365	19970320
AU 730198	B2	20010301		
GB 2326642	A1	19981230	GB 1998 17461	19970320
GB 2326642	B2	20010207		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

PRIORITY APPLN. INFO.: [illegible]
    GB 1996 64[illegible] A 1996[illegible]424
    GB 1998 17461 A3 19970320
    WO 1997 GB783 W 19970320

AB The invention provides a method of detg. whether a **peptide** of a protein is a cryptic **peptide** [illegible] The method includes [illegible] **peptide** [illegible] **peptide** [illegible] **peptide** [illegible] challenge [illegible] the T cells [illegible] the protein and measuring the reactivity of the pre challenged T cells with the **peptide** in the secondary challenge of step iii , and the **peptide** is a cryptic **peptide** if T cell reactivity is observable in the secondary challenge but not in the primary challenge. The cryptic **peptide**

or protein includes **Fel d** I, Der p I, Der p II, Der f I, Der f II, or other allergenic protein derived from grass, tree, weed pollens, fungi, molds, foods, insects, chironomidae, spiders, mites, mammals, latex, biol. detergent additives, and **drugs**.

AB The invention provides a method of detg. whether a **peptide** of a protein is a cryptic **peptide** or protein. The method includes the steps of: i) exposing T cells with the **peptide** in a primary challenge; ii) measuring the reactivity of T cells with the **peptide** in the primary challenge of step i); iii) exposing pre-challenged T cells with the **peptide** in a secondary challenge, wherein the pre-challenged T cells are obtainable by exposing the T cells to the protein; and measuring the reactivity of the pre challenged T cells with the **peptide** in the secondary challenge of step iii), and the **peptide** is a cryptic **peptide** if T cell reactivity is observable in the secondary challenge but not in the primary challenge. The cryptic **peptide** or protein includes **Fel d** I, Der p I, Der p II, Der f I, Der f II, or other allergenic protein derived from grass, tree, weed pollens, fungi, molds, foods, insects, chironomidae, spiders, mites, mammals, latex, biol. detergent additives, and **drugs**.

IT Allergens
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**Fel d** I (Felis domesticus, I); method uses T lymphocytes or mononuclear cells for screening cryptic **peptide** or protein or allergen for prepn. of medicament or diagnostic of allergy or asthma)

IT Anesthetics
Antibiotics
Bee
Blattaria
Cat (Felis catus)
Chironomidae
Dog (Canis familiaris)
Drugs
Food
Fruit fly
Fungi
Gerbil
Grass (Poaceae)
Guinea pig (Cavia porcellus)
Honeybee
Hornet
Horse (Equus caballus)
Housefly (Musca domestica)
Insect (Insecta)
Latex
Mammal (Mammalia)
Mite and Tick
Mold (fungus)
Mouse
Oestrus ovis
Pollen
Rat
Silkworm
Spider
Tenebrio
Tenebrio molitor
Tree
Wasp
Weevil
(allergen; method uses T lymphocytes or mononuclear cells for screening cryptic peptide or protein or allergen for prepn. of medicament or diagnostic of allergy or asthma)

IT 136796-93-5, 23-92 Glycoprotein TRFP (Felis catus chain 1 isoform A protein moiety reduced 197317 08-1, Allergen **Fel d** 1 (Felis catus chain 2)
RL: PRP (Properties)
(amino acid sequence; method uses T lymphocytes or mononuclear cells for screening cryptic **peptide** or protein or allergen for prepn. of medicament or diagnostic of allergy or asthma

L9 ANSWER 14 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
ACCESSION NUMBER: 97112388 EMBASE
DOCUMENT NUMBER: 1997112388
TITLE: Integrated clinical experience with tolerogenic peptides.
AUTHOR: Nicodemus C.; Philip G.; Jones N.; Hirani S.; Norman P.
CORPORATE SOURCE: Dr. C. Nicodemus, Immulogic Pharmaceutical Corporation, 610 Lincoln Street, Waltham, MA 02154, United States
SOURCE: International Archives of Allergy and Immunology, (1997) 113/1-3, 326-328.
Refs: 7
ISSN: 1018-2438 CODEN: IAAIEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

[redacted] peptides [redacted]

[redacted] use regimens containing [redacted] each component **peptide** given in [redacted] been seen with higher doses. Immediate hypersensitivity to treatment **peptides** is rarely seen and can be avoided through patient screening. A putative pathway resulting in histamine mediated but IgE independent allergic symptoms, similar in nature and severity to natural allergen exposure, has been identified in association with [redacted] will be followed in longer term studies.

AB [redacted] been dosed in the clinical development programs for Allervax.RTM. Rat and Ragweed products in North America, Europe and Japan. Two **peptides** derived from **Fel d** 1 and three **peptides** derived from Amb a 1 were selected for clinical

development following T cell epitope mapping of these major allergens. Clinical activity has been demonstrated in several dose regimens containing 75 and 750 mcg of each component **peptide** given in 4-6 doses over 2-4 weeks. Greater activity has been seen with higher doses. Immediate hypersensitivity to treatment **peptides** is rarely seen and can be avoided through patient screening. A putative pathway resulting in histamine mediated but IgE independent allergic symptoms, . . .

CT Medical Descriptors:
***allergy: DT, drug therapy**
conference paper
europe
human
japan
north america
priority journal
***allergen: DT, drug therapy**
***ragweed antigen: DT, drug therapy**
allervax: DT, drug therapy
unclassified drug

L9 ANSWER 15 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:144034 BIOSIS
DOCUMENT NUMBER: PREV199799443237
TITLE: Multicenter study of several doses of ALLER-VAX cat peptides in the treatment of cat allergy.
AUTHOR(S): Norman, P. S. (1); Nicodemus, C. F.; (usa) Allervax Cat Study Group
CORPORATE SOURCE: (1) Johns Hopkins Univ., Baltimore, MD USA
SOURCE: Journal of Allergy and Clinical Immunology (1997) Vol. 99, No. 1 PART 2, pp. S127.
Meeting Info.: Joint Meeting of the American Academy of Allergy, Asthma and Immunology the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997
ISSN: 0091-6749.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English
IT Miscellaneous Descriptors
ALLER-VAX; ALLERGY; ANTIALLERGIC-**DRUG**; CAT ALLERGEN; CAT ALLERGY; CAT **PEPTIDES**, DIAGNOSTIC METHOD; **DRUG** EFFICACY **DRUG** SAFETY, **FEL D 1** IMMUNE SYSTEM DISEASE; MULTICENTER STUDY; PATIENT; **PEPTIDE** PRICK TEST; PHARMACOLOGY; RESPIRATORY ALLERGIC SYMPTOMS

L9 ANSWER 16 OF 24 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97137441 MEDLINE
DOCUMENT NUMBER: 97137441 PubMed ID: 8982778
TITLE: **Fel d 1 peptides** effect on skin tests and cytokine synthesis in cat allergic human subjects.
AUTHOR: Simons F E; Imada M; Li Y; Watson W T; HayGlass K T
CORPORATE SOURCE: Health Sciences Clinical Research Centre, Faculty of Medicine, University of Manitoba, Canada.
SOURCE: INTERNATIONAL IMMUNOLOGY, 1996 Dec, 8 (12) 1937-45.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970318
AB We tested **peptide** immunotherapy in cat-allergic humans using a formation of two synthetic **peptides**, IPC 1 and IPC 2, each of which is 27 amino acids long and contains T cell reactive regions of **Fel d** 1, the major cat allergen. In this exploratory, randomized, double blind, parallel group study, 42 subjects received s.c. injections of treatment **peptides** 250 micrograms or placebo weekly for four consecutive weeks. Changes in immediate and late phase skin test reactivity, and in antigen **driven** cytokine synthesis were assessed. Epicutaneous end point titration and intradermal tests were performed with cat extract ALK-SQ Cat Hair containing **Fel d** 1, before the first injection, then 2, 6 and 24 weeks after the fourth and last injection of **peptides** or placebo. IL 4, IL 10 and IFN gamma expression by circulating peripheral blood mononuclear cells (PBMC) in response to cat extract was measured using short term bulk culture of PBMC and short term limiting dilution analysis. Subjects who received **peptide** immunotherapy did not tolerate significantly more cat extract containing **Fel d** 1 in the skin tests 2, 6 or 24 weeks after the last injection than they did at baseline, and their late phase responses did not decrease significantly compared to baseline. Substantial IL 4, IL 10 and IFN gamma responses were observed following primary culture of cat antigen stimulated PBMC, however, the intensity of cytokine synthesis and the IFN gamma: IL 4 ratio were unchanged in **peptide** and placebo treated groups 6 and 24 weeks

peptide
Fel d
production significantly
Fel d 1 **peptides**:
cytokine synthesis in cat allergic human
AB We tested **peptide** immunotherapy in cat allergic humans using a formation of two synthetic **peptides**, IPC 1 and IPC 2, each of which is 27 amino acids long and contains T cell reactive regions of **Fel d** 1, the major cat allergen. In this exploratory
peptides
driven
were performed with cat extract ALK-SQ Cat Hair containing **Fel d** 1, before the first injection, then 2, 6 and 24 weeks after the fourth and last injection of **peptides** or placebo. IL 4, IL 10 and IFN gamma expression by circulating peripheral blood mononuclear cells (PBMC) in response to cat extract was measured using short term bulk culture of PBMC and short term limiting dilution analysis. Subjects who

received **peptide** immunotherapy did not tolerate significantly more cat extract containing **Fel d** 1 in the skin tests 2, 6 or 24 weeks after the last injection than they did at baseline, and. . . primary culture of cat antigen stimulated PBMC; however, the intensity of cytokine synthesis and the IFN gamma: IL 4 ratio were unchanged in **peptide** and placebo treated groups 6 and 24 weeks after the last injection. A few hours after the injections, subjects receiving **peptides** reported more allergic rhinitis and asthma symptoms and more pruritus than those receiving placebo We conclude that under the conditions tested, **peptide** immunotherapy did not reduce immediate or late phase skin reactivity to cat extract containing **Fel d** 1 or modify cat antigen specific cytokine production significantly.

CT Check Tags: Animal: Female; Human; Male; Support, Non U S. Gov't
Adult
*Asthma: TH, therapy
*Cats: IM, immunology
*Cytokines BI, biosynthesis
***Cytokines: DE, drug effects**
Double Blind Method
Glycoproteins: IM immunology
*Glycoproteins: PD pharmacology
*Immunotherapy: MT methods
Peptide Fragments IM, immunology
*Peptide Fragments . . .

L9 ANSWER 17 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B V.
ACCESSION NUMBER: 97002174 EMBASE
DOCUMENT NUMBER 1997002174
TITLE: Treatment of cat allergy with T cell reactive peptides.
AUTHOR: Norman P.S.; Ohman J.L. Jr.; Long A.A.; Creticos P.S.; Gefter M.A.; Shaked Z.; Wood R.A.; Eggleston P.A.; Hafner K B ; Rao P.; Lichtenstein L.M.; Jones N H.; Nicodemus C.F.
CORPORATE SOURCE: Dr. P.S. Norman, Johns Hopkins Asthma/Allergy Ctr., 5501 Hopkins Bayview Circle, Baltimore, MD 21224-6801, United States
SOURCE: American Journal of Respiratory and Critical Care Medicine, (1996) 154/6 (1623-1628 .
ISSN: 1073 449X CODEN: AJCMED
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We induced in allergic humans the counterpart of murine experimental T-cell tolerance. T cell lines from cat allergic humans were used to map T-cell epitopes for the principal allergen of cat dander, **Fel d** 1. Two **peptides** of 27 amino acids each were synthesized to contain the dominant epitopes ALLERVAX.PTM. CAT). After a safety trial, we carried out a blinded study of the dose required for efficacy. We randomly divided 95 cat sensitive patients into placebo, 7.5 .mu.g, 75 .mu.g, and 750 .mu.g groups. Patients received a subcutaneous injection weekly for 4 wk. Before and after treatment, patients were exposed in a room inhabited by live cats and scored by nose and lung symptoms. Baseline nasal and lung scores .+ SEM: were 6.2 .+ . 0.56 and 5.4 .+ . 0.73 in the 750 .mu.g group; 7.8 .+ . 0.53 and 4.7 .+-. 0.68 in the placebo group. Six weeks after treatment, scores adjusted for baseline differences were reduced in the 750 .mu.g group: -2.3 .+ . 4.9 and -2.3 .+ . 0.59 compared with 0.84 .+ . 0.50 and 0.85 .+-. (.62 in the placebo group. The 75 .mu.g group showed intermediate effects and the 7.5 .mu.g group no effect. Linear trend analysis indicated a significant close response effect: p = 0.05 for nose and 0.03 for lung symptoms. Allergic side effects occurred an hour or more after the first 750 .mu.g dose in 16 of 24 patients but required little or no treatment with one exception. T cell reactive treatment **peptides** safely improved allergic responses to cats.

AB . . . tolerance T cell lines from cat allergic humans were used to map T cell epitopes for the principal allergen of cat dander, **Fel d** 1. Two **peptides** of 27 amino acids each were synthesized to contain the dominant epitopes ALLERVAX.RTM. CAT . After a safety trial, we carried. . . 750 .mu.g dose in 16 of 24 patients but required little or no treatment with one exception. T cell reactive treatment **peptides** safely improved allergic responses to cats.

CT Medical Descriptors:
*allergy: . . . etiology
*allergy: DI, diagnosis
*asthma: DI, diagnosis
*asthma: DM, disease management
*asthma: ET, etiology
*t lymphocyte activation
adult
amino acid synthesis
article
cat
clinical article
clinical trial
[illegible]
drug efficacy
female
[illegible]
human
hypothesis
immunoglobulin blood level
immunological tolerance
lymphocyte proliferation
male
[illegible]
[illegible]
[illegible]
subcutaneous drug administration
[illegible]
*allergen
*allervax cat: CT, clinical trial
***allervax cat: AD, drug administration**
***allervax cat: DO, drug dose**
*peptide: CT, clinical trial

***peptide: AD, drug administration**
***peptide: DO, drug dose**
epitope
immunoglobulin e· EC, endogenous compound
placebo
unclassified drug

L9 ANSWER 18 OF 24 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:144806 BIOSIS
DOCUMENT NUMBER: PREV199698716941
TITLE: **Fel d 1 peptides** (Allervax Cat) in cat allergic subjects.
AUTHOR(S): Simons, F. E. R.; Watson, W. T. A.; Dilay, D. J.; Gillespie, C. A.; Imada M.; Hayglass, K. T.
CORPORATE SOURCE: Winnipeg Canada
SOURCE: Journal of Allergy and Clinical Immunology, (1996) Vol. 97, No. 1 PART 3, pp. 230.
Meeting Info: Fifty second Annual Meeting of the American Academy of Allergy Asthma and Immunology New Orleans, Louisiana USA March 15 20, 1996
ISSN: 0091 6749.
DOCUMENT TYPE: Conference
LANGUAGE: English
TI **Fel d 1 peptides** (Allervax Cat) in cat-allergic subjects.
IT Miscellaneous Descriptors
ALLERGIC RHINITIS; ALLERVAX CAT; ANTIALLERGIC **DRUG**; ASTHMA; INTERFERON-GAMMA; INTERLEUKIN 10; INTERLEUKIN-4; MEETING ABSTRACT; PERIPHERAL BLOOD MONONUCLEAR CELLS; TREATMENT

L9 ANSWER 19 OF 24 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 94194185 MEDLINE
DOCUMENT NUMBER: 94194185 PubMed ID: 8144980
TITLE: Characterization of cat dander-specific T lymphocytes from atopic patients.
AUTHOR: van Neerven R J; van de Pol M M; van Milligen F J; Jansen H M; Aalberse R C; Kapsenberg M L
CORPORATE SOURCE: Laboratory of Cell Biology and Histology, University of Amsterdam, The Netherlands.
SOURCE: JOURNAL OF IMMUNOLOGY, (1994 Apr 15) 152 (8) 4203-10.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940511
Last Updated on STN: 19940511
Entered Medline: 19940505
AB **Fel d** I, the major cat dander allergen, is recognized by serum IgE of more than 80% of all cat allergic patients. Because IgE synthesis by B lymphocytes is under the control of T lymphocytes, we studied the specificity and lymphokine production profiles of cat dander-specific T lymphocytes. Polyclonal cat dander specific T cell lines were found to react with purified **Fel d** I, but not with cat albumin, the only other characterized cat allergen. Similarly, within a panel of CD4+ T lymphocyte clones (TLC) that was generated from these cat dander specific T cell lines, 5 of 16 TLC were found to react with **Fel d** I, and 0 of 16 with cat albumin. The remaining 11 TLC were shown to recognize at least two different proteins. In general, the TLC had a high IL-4/IFN gamma production ratio, and could recognize the cat dander extract in an HLA-**DR**, HLA DQ, or HLA DP restricted manner. In addition, five distinct T cell epitopes of **Fel d** I were identified by using a panel of overlapping synthetic **peptides** of both chains of **Fel d** I. The data presented here indicate that, even though multiple proteins in cat dander extract are recognized by T lymphocytes of allergic patients, **Fel d** I, the major IgE binding allergen, is also important in T cell activation. The fact that the cat specific TLC are Th2 like indicates that these cells may play an important role in the pathophysiology of allergic responses to cat allergens. However, the diversity of HLA class II restriction of cat dander and **Fel d** I specific TLC and the presence of multiple T cell epitopes in the allergen may complicate future immunotherapies.
AB **Fel d** I, the major cat dander allergen, is recognized by serum IgE of more than 80% of all cat allergic patients. Because, . . . lymphokine production profiles of cat dander specific T lymphocytes. Polyclonal cat dander specific T cell lines were found to react with purified **Fel d** I, but not with cat albumin, the only other characterized cat allergen. Similarly, within a panel of CD4+ T lymphocyte. . . . TLC that was generated from these cat dander-specific T cell lines, 5 of 16 TLC were found to react with **Fel d** I, and 0 of 16 with cat albumin. The remaining 11 TLC were shown to recognize at least two different. . . . proteins. In general, the TLC had a high IL 4/IFN gamma production ratio and could recognize the cat dander extract in an HLA **DR**, HLA DQ, or HLA DP restricted manner. In addition, five distinct T cell epitopes of **Fel d** I were identified by using a panel of overlapping synthetic **peptides** of both chains of **Fel d** I. The data presented here

[illegible]

L9 ANSWER 20 OF 24 EMBASE COPYRIGHT [illegible] ELSEVIER [illegible]
ACCESSION NUMBER: 94289031 EMBASE
DOCUMENT NUMBER: 1994289031
TITLE: Potential therapeutic [illegible]

[illegible]

SOURCE: Molecular Immunology, [illegible]
ISSN: [illegible]
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The complete primary structure of **Fel d** I2 has been determined and shown to be comprised of two separate polypeptide chains (designated chain 1 and chain 2). Overlapping **peptides** covering the entire sequence of both chains of **Fel d** I have been used to map the major areas of human T cell reactivity. The present study describes three non contiguous T cell reactive regions of <30 aa in length that were assembled in all six possible configurations using PCR and recombinant DNA methods. These six recombinant proteins comprised of defined non contiguous T cell epitope regions artificially combined into single polypeptide chains have been expressed in E. coli, highly purified, and examined for their ability to bind to human cat allergic IgE and for human T cell reactivity. Several of these recombined T cell epitope-containing polypeptides exhibit markedly reduced IgE binding as compared to the native **Fel d** I. Importantly, the human T cell reactivity to individual T cell epitope containing regions is maintained even though each was placed in an unnatural position as compared to the native molecule. In addition, T cell responses to potential junctional epitopes were not detected. It was also demonstrated in mice that s.c. injection of T cell epitope-containing polypeptides inhibits the T cell response to the individual **peptides** upon subsequent challenge in vitro. Thus, these recombined T cell epitope containing polypeptides, which harbor multiple T cell reactive regions but have significantly reduced reactivity with allergic human IgE, constitute a novel potential approach for desensitization to important allergens.

AB The complete primary structure of **Fel d** I2 has been determined and shown to be comprised of two separate polypeptide chains (designated chain 1 and chain 2). Overlapping **peptides** covering the entire sequence of both chains of **Fel d** I have been used to map the major areas of human T cell reactivity. The present study describes three non-contiguous . . . cell reactivity. Several of these recombined T cell epitope containing polypeptides exhibit markedly reduced IgE binding as compared to the native **Fel d** I. Importantly, the human T cell reactivity to individual T cell epitope-containing regions is maintained even though each was placed. . . . also demonstrated in mice that s.c. injection of T cell epitope-containing polypeptides inhibits the T cell response to the individual **peptides** upon subsequent challenge in vitro. Thus, these recombined T cell epitope containing polypeptides, which harbor multiple T cell reactive regions but . . .

CT Medical Descriptors:
*cell proliferation
*t lymphocyte
amino acid sequence
article
controlled study
human
priority journal
*epitope
*polypeptide: PD, pharmacology
***polypeptide: DV, drug development**
*recombinant protein PD pharmacology
***recombinant protein: DV, drug development**

L9 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:595663 CAPLUS
DOCUMENT NUMBER: 119:195663
TITLE: Histamine derivatives as immunomodulators and in immunotherapeutics
INVENTOR(S): Greenstein, Julia L.; Melmon, Kenneth L
PATENT ASSIGNEE(S): Immulogic Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313772	A1	1993[illegible]	WO 1993 US664	19930119
W: AU, CA, FI, [illegible]				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9335917	A1	19930803	AU 1993 35917	19930119
EP 621780	A1	19941102	EP 1993 904617	19930119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503239	T2	19950406	JP 1993 512737	19930119
CN 1078153	A	19931110	CN 1993 102512	19930121

PRIORITY APPLN. INFO.: US 1992 823229 19920121
WO 1993 US664 19930119
OTHER SOURCE(S): MARPAT 119:195663

AB Histamine derivs. Hi[illegible] NHX CH2 nY. HA [illegible] (X = CO, CHR; Y = Me, CONHZ; A = counter ion; R = C1-3 alkyl; Z = H, CH2 mMe, un substituted Ph; m = 1 4; [illegible] is useful for treatment of antigen sensitivity in [illegible]

[illegible]

humans. The compds. may be administered in conjunction with the antigen and/or with a **peptide** having T cell stimulating activity derived from the antigen. Mice immunized with His NHCHMe CH2 4CONHC6H4CF3 (100 mg/kg) had no IgG or IgE response to **Fel d** I antigen (isolated from the house dust from homes with cats). [illegible]

[illegible]

TITLE: [illegible] **peptides** [illegible] the major cat allergen **Fel d** I.
AUTHOR: Briner T [illegible] Keating K M; Rogers B L; Greenstein J L
CORPORATE SOURCE: Immulogic Pharmaceutical Corp., Waltham, MA 02154.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, 1993 Aug 15 90 16 7608-12. Journal code 7505876. ISSN: 0027 8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199310
ENTRY DATE: Entered STN: 19931008
Last Updated on STN: 19931008
Entered Medline: 19930923

AB T cells control the majority of antigen specific immune responses. Therefore, influencing the activation of the T cell response in order to modify immune responsiveness is an obvious therapeutic goal. We have used a mouse model of response to **Fel d** I, the major cat protein allergen in humans, to explore the ability of **peptides** derived from **Fel d** I to inhibit T cell dependent immune responses to the **peptides** themselves and to larger polypeptides. T cells from B6CBAF1 mice respond to the **Fel d** I **peptide** IPC 1 after challenge with IPC 2. However, subcutaneous tolerization with IPC 1 prevents this response as measured by production of interleukins 2 and 4 and interferon gamma. **Fel d** I immunization of B6D2F1 mice results in T-cell responses primarily to one **peptide** derived from **Fel d** I. Injecting this **peptide** in soluble form inhibits T cell activation (as measured by interleukin 2 production) and antibody production in **Fel d** I primed animals when they are subsequently challenged with **peptide** in adjuvant. Most of the cat allergic human T cell response to **Fel d** I is specific for two **peptides** on one of its two chains. Immunization of B6CBAF1 mice with recombinant **Fel d** I chain 1 results in T cell responses to the same **peptides**. Subcutaneous administration of these two **peptides**, which contain some, but not all, of the T cell epitopes from **Fel d** I chain I, decreases the T cell response to the entire recombinant **Fel d** I chain 1. The ability to tolerize T cell responses with subcutaneous injections suggests a practical approach to treating human diseases with **peptides** containing T cell epitopes.

TI Peripheral T-cell tolerance induced in naive and primed mice by subcutaneous injection of **peptides** from the major cat allergen **Fel d** I.

AB . . . in order to modify immune responsiveness is an obvious therapeutic goal. We have used a mouse model of response to **Fel d** I the major cat protein allergen in humans, to explore the ability of **peptides** derived from **Fel d** I to inhibit T-cell-dependent immune responses to the **peptides** themselves and to larger polypeptides. T cells from B6CBAF1 mice respond to the **Fel d** I **peptide** IPC 1 after challenge with IPC-2. However subcutaneous tolerization with IPC 2 prevents this response as measured by production of interleukins 2 and 4 and interferon gamma. **Fel d** I immunization of B6D2F1 mice results in T cell responses primarily to one **peptide** derived from **Fel d** I. Injecting this **peptide** in soluble form inhibits T cell activation (as measured by interleukin 2 production) and antibody production in **Fel d** I primed animals when they are subsequently challenged with **peptide** in adjuvant. Most of the cat allergic human T cell response to **Fel d** I is specific for two **peptides** on one of its two chains. Immunization of B6CBAF1 mice with recombinant **Fel d** I chain 1 results in T cell responses to the same **peptides**. Subcutaneous administration of these two **peptides**, which contain some, but not all, of the T cell epitopes from **Fel d** I chain I, decreases the T cell response to the entire recombinant **Fel d** I chain 1. The ability to tolerize T cell responses with subcutaneous injections suggests a practical approach to treating human diseases with **peptides** containing T cell epitopes.

CT . . .
biosynthesis
Interleukin 2: BI, biosynthesis
Interleukin 4: BI, biosynthesis
Lymph Nodes: IM, immunology
Mice
*Mice, Inbred Strains: IM, immunology
Spleen: IM, immunology
T-Lymphocytes: DE, drug effects
*T Lymphocytes: IM, immunology

L9 ANSWER 23 OF 24 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 93384 81 MEDLINE
DOCUMENT NUMBER: 93384 81 PubMed ID: 8373007
TITLE: Therapeutic potential of peptides in allergic disease.
AUTHOR: Norman P S
CORPORATE SOURCE: Johns Hopkins Asthma and Allergy Center, Baltimore, Maryland.
SOURCE: ANNALS OF ALLERGY, 1993 Sep 71 3 330 3. Ref: 10 Journal code: 0372346. ISSN: 0003 4738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; JOURNAL ARTICLE

[illegible]

AB Immunotherapy with [illegible] in many patients, but its effects are temporary and variable. This type of intervention provokes a transient increase in IgE antibody synthesis that may produce untoward side effects. Recent research has suggested that such immunotherapy downregulates T cell activity, indicating that regulation of [illegible] **peptides**
Peptides [illegible]
Although evidence [illegible] was noted, allergic reactions occurred [illegible] researchers synthesized **peptides** representing short sequences from the protein chains of principal allergens such as Amb a I of ragweed and **Fel d** I of cat. Assays of proliferation of T cell lines from ragweed and cat sensitive patients have shown that relatively short sequences from

these proteins are responsible for a major portion of the activity of the whole protein. One such cat **peptide** has shown no reactivity with human IgE. The characteristics of these **peptides** suggest they should be evaluated further in clinical trials of allergic patients. The anticipated outcome would be prolonged T cell downregulation, which might result in suppression of late phase allergic inflammation and IgE antibody synthesis. The question whether such changes will reduce clinical reactivity sufficiently to be clinically useful remains to be answered in future studies.

AB . . . . the therapeutic response. Animal studies have shown that T cells can be rendered anergic by the administration of nonimmunogenic, T cell active **peptides**. **Peptides** prepared by urea denaturation of purified allergens and by pepsin digestion of crude allergens have been evaluated in humans. Although evidence of specific immunosuppression was noted allergic reactions occurred as well. Subsequently, researchers synthesized **peptides** representing short sequences from the protein chains of principal allergens, such as Amb a I of ragweed and **Fel d** I of cat. Assays of proliferation of T cell lines from ragweed and cat sensitive patients have shown that relatively short sequences from these proteins are responsible for a major portion of the activity of the whole protein. One such cat **peptide** has shown no reactivity with human IgE. The characteristics of these **peptides** suggest they should be evaluated further in clinical trials of allergic patients. The anticipated outcome would be prolonged T cell downregulation. . . .

CT Check Tags: Human

***Hypersensitivity: DT, drug therapy**
Immunotherapy
*Peptides: TU, therapeutic use
T-Lymphocytes: DE, drug effects
T-Lymphocytes: IM, immunology

L9 ANSWER 24 OF 24 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: [illegible] EMBASE
DOCUMENT NUMBER: [illegible]
TITLE: Immunotherapy of allergic disorders: Traditional and novel approaches.
AUTHOR: Franklin Adkinson Jr. N.; Hamilton R.G.; Creticos P.S.; Lichtenstein L.M. Norman P.S.
CORPORATE SOURCE: Johns Hopkins University, Baltimore, MD 21224, United States
SOURCE: International Archives of Allergy and Immunology, (1992) 99 2-4 (317-320)
ISSN: 1018-2438 CODEN: IAAIEG
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB For approaches to the immunotherapy of allergic respiratory diseases now under study at Johns Hopkins are reviewed. Traditional high dose parenteral immunization with mixtures of allergens corresponding to patients' allergic sensitivities is being evaluated in the long term management of allergic asthma in children. Oral desensitization employing doses of short ragweed extract 100 fold higher than for parenteral therapy has been proven safe and efficacious and is now being modified to render it practicable. Intradermal injections of autologous IgG immune complexes with D. pteronyssinus antigens has been reported to improve symptoms and reduce IgE synthesis; a trial to replicate these findings is underway. Immunization with immunodominant **peptides** from **Fel d.** I is also under development as a novel immunoregulatory intervention with potential clinical application.

AB . . . . been reported to improve symptoms and reduce IgE synthesis; a trial to replicate these findings is underway. Immunization with immunodominant **peptides** from **Fel d.** I is also under development as a novel immunoregulatory intervention with potential clinical application.

CT Medical Descriptors:

***allergic disease: DT, drug therapy**
*allergic disease: PC, prevention
*immunotherapy
allergic asthma: DT, drug therapy
allergic asthma: PC, prevention
antigen antibody complex
conference paper
desensitization
human
immunization
immunoglobulin production
intradermal drug administration
oral drug administration
priority journal
ragweed
respiratory tract disease: PC, prevention
respiratory tract disease: DT, drug therapy
allergen: DT, drug therapy
immunoglobulin e: [illegible] endogenous compound
immunoglobulin g antibody: DT, drug therapy
plant extract: DT, drug therapy

[illegible]

L3 [illegible]
L4 18 [illegible]
L5 10 [illegible] PEM [illegible]
L6 916 [illegible]

PROCESSING [illegible]
L11 [illegible]

=> dis l11 1 3 ibib abs kwic

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:444999 CAPLUS
DOCUMENT NUMBER: 131:87873
TITLE: Methods and compositions for desensitization
INVENTOR(S): Larche, Mark; Kay, Anthony Barrington
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9934826	A1	19990715	WO 1999 GB80	19990111
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2317724	AA	19990715	CA 1999 2317724	19990111
AU 9920648	A1	19990726	AU 1999 20648	19990111
EP 1044019	A1	20001018	EP 1999 901014	19990111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
GB 2348808	A1	20001018	GB 2000 16438	19990111
JP 2002500199	T2	20020108	JP 2000 527273	19990111

PRIORITY APPLN. INFO.: GB 1998 445 A 19980109
GB 1998 20474 A 19980921
WO 1999 GB80 W 19990111

AB A method of desensitizing a patient to a polypeptide allergen the method comprising administering to the patient a peptide derived from the allergen wherein restriction to a MHC Class II mol. possessed by the patient can be demonstrated by the peptide and the peptide is able to induce a **late phase response** in an individual who possesses the said MHC Class II mol. A compn. comprising a plurality of peptides derived from a polypeptide allergen wherein for at least one of the peptides in the compn. restriction to a MHC Class II mol. can be demonstrated, and the compn. is able to induce a **late phase response** in an individual possessing the given MHC Class II mol. The invention also relates to a method of selecting a peptide for use as an immunotherapeutic agent for desensitizing a patient to a polypeptide allergen capable of eliciting an allergic response in the patient, which patient possesses a particular MHC Class II mol., the method comprising the steps of (1) selecting a candidate peptide derived from the polypeptide allergen, (2) detg. whether the candidate peptide demonstrates restriction to the said MHC Class II mol., and (3) detg. whether the candidate peptide is able to induce a **late phase response** in an individual who possesses the said MHC Class II mol.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A method of desensitizing a patient to a polypeptide allergen the method comprising administering to the patient a peptide derived from the allergen wherein restriction to a MHC Class II mol. possessed by the patient can be demonstrated by the peptide and the peptide is able to induce a **late phase response** in an individual who possesses the said MHC Class II mol. A compn. comprising a plurality of peptides derived from a polypeptide allergen wherein for at least one of the peptides in the compn. restriction to a MHC Class II mol. can be demonstrated, and the compn. is able to induce a **late phase response** in an individual possessing the given MHC Class II mol. The invention also relates to a method of selecting a peptide for use as an immunotherapeutic agent for desensitizing a patient to a polypeptide allergen capable of eliciting an allergic response in the patient, which patient possesses a particular MHC Class II mol., the method comprising the steps of (1) selecting a candidate peptide derived from the polypeptide allergen, (2) detg. whether the candidate peptide demonstrates restriction to the said MHC Class II mol., and (3) detg. whether the candidate peptide is able to induce a **late phase response** in an individual who possesses the said MHC Class II mol.

ST **Fel d** I allergen [illegible] desensitization immunotherapy MHC II [illegible] **peptide** desensitization

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
Der f I (Dermatophagoides farinae, I); compns. comprising **Fel d** I allergen epitope **peptides** for desensitization

IT Allergens
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
[illegible]
Fel d [illegible] peptides
desensitization

IT Allergens
RL: BSU (Biological [illegible] unclassified); PRP (Properties); THU (Therapeutic use); [illegible] (Biological study); USES (Uses)
Der p II (Dermatophagoides pteronyssinus II); compns. comprising **Fel d** [illegible] peptides
[illegible]
Fel d [illegible]
Fel d [illegible] peptides
desensitization

IT Histocompatibility [illegible]
RL: BPR (Biological [illegible] Biological study, unclassified); BIOL (Biological study); [illegible]

(HLA DP; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DQ; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DR2; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DR3; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DR4; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DR7; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(HLA DR; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Histocompatibility antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(MHC (major histocompatibility complex) class II; compns. comprising
Fel d I allergen epitope **peptides** for
desensitization)

IT Bioassay
(T cell proliferation; compns. comprising **Fel d** I
allergen epitope peptides for desensitization)

IT Cell proliferation
(T cell, bioassay; compns. comprising **Fel d** I
allergen epitope peptides for desensitization)

IT Worm
(allergen of [illegible]; compns. comprising **Fel d** I
allergen epitope peptides for desensitization)

IT Bee
Beetle (Coleoptera)
Blattaria
Calliphora vicina
Calliphoridae
Cat (Felis catus)
Cattle
Chironomidae
Dog (Canis familiaris)
Food
Fruit fly
Fungi
Gerbil
Grass (Poaceae)
Guinea pig (Cavia [illegible])
Honeybee
Horse (Equus caballus)
Housefly (Musca [illegible])
Mammal (Mammalia)
Mite and Tick
Mold (fungus)
Moth
Mouse
Pollen
Rabbit
Ragweed (Ambrosia)
Rat
Sheep
Silkworm
Spider
Swine
Tree
Weed
Weevil
(allergens; compns. comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT Tenebrio molitor
(beetle allergen; compns. comprising **Fel d** I
allergen epitope peptides for desensitization)

IT Allergy
Drug delivery systems
Immunotherapy
[illegible]
peptides [illegible]

IT [illegible]
(fly allergen; [illegible] comprising **Fel d** I allergen
epitope **peptides** for desensitization)

IT T cell (lymphocyte)
(proliferation; [illegible] compns. comprising **Fel d**
[illegible]
pep[illegible]
[illegible] **Fel d** [illegible]
allergen epitope peptides for desensitization)

IT 136794-3[illegible] [illegible] Felis catus chain 1 isoform A
protein moiety [illegible] 197169-34-1 [illegible] 197170-[illegible]-6
197170-[illegible] [illegible] 197170-34-[illegible] 197170-36-8
229720-52-4 [illegible] 229720-55-[illegible] 229720-56-8

229020-57-9 [illegible] 229120-59-1 229173-24-4
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising **Fel d** 1 allergen epitope **peptides** for [illegible])

L11 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: [illegible] BIOSIS
DOCUMENT NUMBER: [illegible]38033
TITLE: Attenuation of bronchial and cutaneous allergic **late phase responses** by allergen derived peptides.
AUTHOR(S): [illegible], W. L. G. (1); Shirley, K. E. (1); Haselden, B. M. (1); [illegible], M. (1); Kay, A. B. (1)
CORPORATE SOURCE: (1) Allergy and Clinical Immunology, ICSM at NHLI, [illegible] Street, London, SW3 6LY UK
SOURCE: [illegible], (Dec., 1999) Vol. 98, No. suppl. 1, pp. 40.
Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology Harrogate, England UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology
[illegible] 19-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

TI Attenuation of bronchial and cutaneous allergic **late phase responses** by allergen derived peptides

IT [illegible]
and Homeostasis, [illegible]

IT Diseases
allergy: [illegible] disease, asthma: immune system disease, respiratory system disease

IT Chemicals & Biochemicals
Fel d 1: allergen; **Fel d 1**
peptide: antiallergic agent

IT Alternate Indexing
Hypersensitivity (MeSH); Asthma (MeSH)

L11 ANSWER 3 OF 3 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 97[illegible] MEDLINE
DOCUMENT NUMBER: 97[illegible] PubMed ID: 8982778
TITLE: **Fel d 1 peptides**: effect on skin tests and cytokine synthesis in cat-allergic human subjects.
AUTHOR: Simons F E; Imada M; Li Y; Watson W T; HayGlass K T
CORPORATE SOURCE: Health Sciences Clinical Research Centre, Faculty of Medicine, University of Manitoba, Canada.
SOURCE: INTERNATIONAL IMMUNOLOGY, (1996 Dec) 8 (12) 1937-45.
Journal code: 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970318

AB We tested **peptide** immunotherapy in cat allergic humans, using a formulation of two synthetic **peptides** (IPC-1 and IPC-2), each of which is 27 amino acids long and contains T cell reactive regions of **Fel d 1**, the major cat allergen. In this exploratory, randomized, double blind, parallel group study, 42 subjects received s.c. injections of treatment **peptides** 250 micrograms or placebo weekly for four consecutive weeks. Changes in immediate and late phase skin test reactivity, and in antigen driven cytokine synthesis were assessed. Epicutaneous endpoint titration and intradermal tests were performed with cat extract (ALK SQ Cat Hair) containing **Fel d 1**, before the first injection, then 2, 6 and 24 weeks after the fourth and last injection of **peptides** or placebo. IL-4, IL-10 and IFN gamma expression by stimulating peripheral blood mononuclear cells (PBMC) in response to cat extract was measured using short term bulk culture of PBMC and short term limiting dilution analysis. Subjects who received **peptide** immunotherapy did not tolerate significantly more cat extract containing **Fel d 1** in the skin tests 2, 6 or 24 weeks after the last injection than they did at baseline, and their **late phase responses** did not decrease significantly compared with baseline. Substantial IL-4, IL-10 and IFN gamma responses were observed following primary culture of cat antigen stimulated PBMC. However, the intensity of cytokine synthesis and the IFN gamma: IL-4 ratio were unchanged in **peptide** and placebo treated groups up to 24 weeks after the last injection. A few hours after the injections, subjects receiving **peptides** reported more allergic rhinitis and asthma symptoms and more pruritus than those receiving placebo. We conclude that under the conditions tested, **peptide** immunotherapy did not reduce immediate or late phase skin reactivity to cat extract containing **Fel d 1** or modify cat antigen specific [illegible] significantly.

[illegible]

Fel d [illegible]
[illegible] **peptides** [illegible]
weekly [illegible] immediate and late phase skin test reactivity, [illegible] cytokine synthesis were assessed. [illegible] titration and intradermal tests were performed with [illegible] (ALK SQ Cat Hair) containing **Fel d 1**, before the first [illegible] then 2, 6 and 24 weeks after the [illegible]
[illegible] **peptide** [illegible]
[illegible] **Fel d 1** [illegible]
2, 6 or 24 weeks after [illegible] than they did at baseline, and their **late phase responses** did not decrease significantly [illegible] IL-4, IL-10 and IFN gamma responses were observed [illegible] primary culture of cat antigen stimulated PBMC [illegible] the intensity of cytokine synthesis and

the IFN gamma: IL 4 ratio were unchanged in **peptide** and
placebo treated groups [illegible] and 24 weeks after the last injection. A few
hours after the injections, subjects receiving **peptides** reported
more allergic rhinitis and asthma symptoms and more pruritus than those
receiving placebo. We conclude that under the conditions tested,
peptide immunotherapy [illegible] reduce immediate or late phase skin
reactivity to cat extract containing **Fel d** 1 or modify
cat antigen specific cytokine production significantly.

=> dis his

(FILE 'HOME' ENTERED AT [illegible] ON 23 AUG 2002

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:19:59 ON 23 AUG 2002
L1 2885 S LARCHE M?/AU OR RAY A?/AU
L2 503 S L1 AND ALLERGEN
L3 56 S L2 AND PEPTIDE
L4 18 S L3 AND MHC OR HLA
L5 10 DUP REM L4 (8 DUPLICATES REMOVED
L6 916 S FEL 1N 1 OR D
L7 125 S L6 (P) PEPTIDE
L8 45 S L7 AND DRB
L9 24 DUP REM L8 (21 DUPLICATES REMOVED
L10 6 S L7 AND (LATE OR PHASE OR RESPONSE)
L11 3 DUP REM L10 (3 DUPLICATES REMOVED)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y /N/HOLD):y
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	106.81	107.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	4.96	-4.96

STN INTERNATIONAL LOGOFF AT [illegible] ON 23 AUG 2002

WEST Search History

DATE: Friday, August 23, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L15	(allergy and (late adj phase adj response)) same peptide$4	0	L15
L14	allergy and (late adj phase adj response)	63	L14
L13	allergy and (late phase response)	10856	L13
L12	(fel adj d adj 1) and DR$4	10	L12
L11	(fel adj d adj 1) and DR$6	10	L11
L10	(fel adj d adj 1) and DR$9	6	L10
L9	(fel adj d adj 1) and DR4	0	L9
L8	(cat adj allergen adj 1)	3	L8
L7	(fel adj d adj 1)	10	L7
L6	L4 and (fel adj d adj 1)	0	L6
L5	L4 (fel adj d adj 1)	29	L5
L4	DR4 and allergen	19	L4
L3	L2 and allergen	4	L3
L2	L1 and MHC	19	L2
L1	(kay)[in] or (larch)[in]	3318	L1

END OF SEARCH HISTORY

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:19:59 ON 23 AUG 2002

L1 2885 S LARCHE M?/AU OR KAY A?/AU
L2 503 S L1 AND ALLERGEN
L3 56 S L2 AND PEPTIDE?
L4 18 S L3 AND (MHC OR HLA
L5 10 DUP REM L4 (8 DUPLICATES REMOVED
L6 916 S (FEL (1N) D (1N) D)
L7 125 S L6 (P) PEPTIDE?
L8 45 S L7 AND DR?
L9 24 DUP REM L8 (21 DUPLICATES REMOVED
L10 6 S L7 AND (LATE (1N) PHASE (1N) RESPONSE)
L11 3 DUP REM L10 (3 DUPLICATES REMOVED)